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Washington State Pharmacy and Therapeutics Committee
Drug Utilization Review Board
October 17, 2012

Barak Gaster: A new member has joined us on the committee. Michael Johnson is… currently serves as the Chair of the Joint P&T Committee for Central Washington Hospital and the Wenatchee Valley Medical Center and is a Board Certified Internist and has expertise in electronic medical records, critical care and quality management. He is also a Licensed Pharmacist having served as a staff pharmacist at Northeast Regional Medical Center and Sacred Heart Medical Center in Spokane. It is a pleasure to have you on the committee. Thank you very much for joining us.

And so let's begin on this end and go around and make introductions.

Nicole Nguyen: I'm Nicole Nguyen, Senior Pharmacist with Medicaid.

Chuck Agte: Chuck Agte, Pharmacy Administrator for Medicaid.

Amy Irwin: Amy Irwin, Washington Medicaid.

Christine Klingel: Christine Klingel, committee member.

Eric Harvey: Eric Harvey, committee member.

Mason Bowman: Mason Bowman, committee member.

Christopher Smith: Christopher Smith, committee member.

Barak Gaster: Barak Gaster, committee member.

Deb Wiser: Deb Wiser, committee member.

Michael Johnson: Michael Johnson, new committee member.

Po Karczewski: Po Karczewski, committee member.

Regina Chacon: Regina Chacon, Health Care Authority.

Leta Evaskus: Leta Evaskus, Health Care Authority.

Donna Sullivan: Donna Sullivan, Health Care Authority.

Duane Thurman: Duane Thurman, Health Care Authority and I just want to point out that Health Care Authority is Medicaid now. So we are all in the same agency and we're going through a transition. And I also want to remind people that we are transcribing and recording the meeting. So please speak into the mike and identify yourselves for the record. Thanks.

Ray Hanley: Ray Hanley, Health Care Authority.

Barak Gaster: All right. And so I think first on our agenda today is Chuck Agte who is going to give us an update on SPA.

Chuck Agte: This is Charles Agte and we have on the agenda today SPA. It is our state plan amendment. Currently we have delay… our last scheduled implementation date for the formulary had been going to be October 1st to implement the first classes you guys had made decisions on. We, at this time, have delayed formulary implementation for the time being because we are going through the process with the federal government, CMS, for approval of our state plan amendment. That's what the CPA is. Because we are… although there is… we don't have to have an approved state plan amendment to move forward with the program. We do, however, want to make sure that we get an approved state plan amendment at some point. And so we're working closely with CMS to achieve an approved state planned amendment before we actually move forward with implementation. So we're still in the process of working out the details of that state planned amendment with CMS.

And we do have a series of questions back from CMS that we are in the process of responding to formally right now. So once we provide our formal response they will continue the review process. There isn't really any danger that we won't have an approved state plan amendment. It's more a matter of timing of when and why and continuing to hammer out details of our implementation with CMS in the process. So right now we're actually pretty close to having an approved state plan amendment, but we're not going to go ahead and actually implement the formulary until we have official approval from CMS.

That's essential the state of the state plan amendment at the moment. Does the board have any questions in regard to the state plan amendment or our plans to delay until we have approval?

Barak Gaster: This is Barak Gaster. Thanks, Chuck. Could you venture a guess at what a new target date for release of the formulary would be?

Chuck Agte: Right now our plan is to implement on the first of the month after receiving CMS approval. And so that could… we have an announcement out there that basically says that could be as early as November 1st. We were to get approval between now and the end of the month realistically, based on the timeframes for our response and then their review, I don't believe it will be November 1st at this point. But it still could be. It's more likely going to be around December 1st would be my impression. But I'm playing [inaudible] there. What the official timeframe is, is that once we provide our response to their official request for information the CMS offices have 90 days after we supply our response to either ask further questions or provide approval based on the information that we've given. So it can be up to 90 days after we get our response back to them. We're expecting to have our response to them next week. CMS is aware that we're trying to keep to a fairly tight timeframe on this. So I don't expect that they would take the full 90 days, but they do have up to 90 days after we provide our response. So it could be as early as November 1st. It could be as late as January or February if they were to need the full 90 days to come to a conclusion on the state plan amendment.

Duane Thurman: This is Duane. If I could just… I just want to point I've been getting a lot of questions this morning about the move to managed care

Medicaid that was taking place and I've confirmed that Nathan Johnson, our Policy Director is the contact that can give you the information on the figures and how that went through. I also want to point out that if you don't know this, that Dr. Jeff Thompson, our Chief Medical Officer, has decided to leave the agency and will be joining Mercer November 1st as a consultant. So we will be without Jeff.

Chuck Agte: In regard to follow-up on the transition to managed care, just don't have a lot of detail because both managed care and eligibility are not my forte. They are well outside the pharmacy. But we do… so for total numbers and volume impact Nathan would be the best contact. But the… at a kind of high level the population that is being transitioned into managed care is the blind and disabled population that are on Medicaid and the… as part of that transition they were phased in in three groups across the state. The first two groups have already transitioned and the final group is transitioning on November 1st. So we have about two-thirds of the transition complete.

Duane Thurman: Do you have any numbers?

Chuck Agte: No, not off hand I don't have them with me. And so I'd rather… I know some vague round numbers, but I'd rather people get real numbers from someone who knows them. And so from there we have the WAC, Washington Administration Code update is also on the agenda here and that is our other, you know, official rule making part of the process besides the state plan amendment. We completed the Washington Administrative Code process of defining what our rules around the… the high level rules around the development of the formulary and our application of that within Medicaid and that was officially filed at the end of September and with an effective date of November 1st because we were originally shooting for November 1st implementation date. So our Washington administrative code will still be effective November 1st, which does not obligate us to implement on that date. It just means that the rules are in place for us to be able to implement formulary classes. So we won't be modifying or… there isn't really a slowdown of the WAC process. We already have the final Washington Administrative Code filed. It's set to become effective November 1st. There have been some questions about are we going to retract that WAC until we have the state plan amendment

approved? And we're not going to. The Washington Administrative Code is solid. It's not directly tied to the state plan amendment process. So it will be technically in effect on November 1st even though we're not implementing the formulary on that date because it's essentially the rules by which we can apply the formulary. That effective date of November 1st doesn't mean that we actually have to have anything effective as non formulary at that time.

Christopher Smith: This is Christopher Smith. I just wanted to get back to what you were saying before about transitioning patients over to the managed care plan. Does that mean that this formulary will apply to a smaller number of Medicaid insured patients? Is that why you're bringing that issue up?

Duane Thurman: That is my impression. But we'll confirm that.

Christopher Smith: And we're talking about a dramatic factor like half as many patients or 10% less; just sort of ballpark or you don't want to estimate?

Chuck Agte: Ballpark wise we're losing I think… because we already within the Medicaid program have dual eligibles are carved who are technically fee-for-service Medicaid clients, but they have their pharmacy benefit through Part D. So we haven't been administering their pharmacy benefit through fee-for-service anyway. So we kind of have a smaller population that the regular fee-for-service clientele anyway. We're losing about half, I would say, of our clients. But we've known this all along. For example, in all of the data that you're show in regard to the formulary; when you look at the utilization data on drug classes that you guys have been reviewing, we've already carved out the population that we know will be in managed care. So it… this isn't new and we've had that planning in place in regard to the formulary for a while. So when you're looking at numbers you're not looking at the… even though it's historical data, you're not looking at all Medicaid clients who are receiving products. You're looking at all Medicaid clients that we know will still be covered under the fee-for-service benefit.

Barak Gaster: This is Barak Gaster. You may not be able to say much about this, but we got an email referring to a legal challenge that was putting a delay on the formulary. Anything anybody can say about the status of that?

Chuck Agte: It's not… Duane might have more to say on it. It's not technically a legal challenge at this point.

Duane Thurman: No. I think what you're referring to is a letter on behalf of some pharmaceutical companies raising issues about concerns they have about the formulary and we just responded to that and I will get a copy to you. But there's been no further action on that and I would not classify it as a legal action. I think it was just pointing out some questions that we've been getting from lots of legislators and others too. So I should have gotten that out to you earlier. I will send that out to you at the end of the meeting.

Barak Gaster: Thank you.

Chuck Agte: So that you know, since you brought it up… part of… in addition to other stakeholder information, additional legal analysis that we've been doing with our AAG there is… so the… (a) it's not a legal challenge. It did bring up some issues that have also been brought up by other people, which is part of some of what we'll be taking a look at as we move forward in the agenda today. Because there have been points raised by various stakeholder groups that we're looking at including CMS where we're looking at refining and fine-tuning the way we're documenting our formulary decisions.

Barak Gaster: Thank you, Chuck. And so I think next on the agenda is Donna to give us an update on the monograph and compendia.

Donna Sullivan: This is Donna Sullivan. So I've been working with our vendor, ODS, and MedImpact on the monographs and we have… I made a schedule now so that we can definitely get our monographs at least 30 days ahead of our meetings. And I'm working with our internal staff to really improve the process with our data getting the cost information to the committee and posted sooner as well. So what we'll be doing now for the drug classes is… at today's meeting we'll be looking at which drug classes we want to bring forward for the February meeting and the December meeting. So I've already identified two classes that I want to do for December that we'll share with you later today at the end of the agenda. But what that does is that gives us enough time for MedImpact to make updates to the monographs, if necessary; take out

their proprietary information that is specific to their book of business and then get it to us in enough time to be able to post it 30 days ahead of time.

As we move forward we'll always be planning for the meeting two meetings away. So it is giving us a four-month window and that hopefully will get us to the point where we are getting information to you in a more timely manner.

We also have gotten approval from our vendor to use the compendia. So we'll be… we are… the staff in pharmacy policy with Medicaid are looking at how we're going to take the information out of Micromedics and the labeling to present that information to the committee for drug classes where we don't have a monograph from MedImpact. So the big thing that I'm looking at right now is how do we insert those studies and is there newer information that has yet to be put into Drug Dex that, you know, we can consider. So we're working with the AGs office in how we are going to present that information to the committee as well. And so I will be bringing that to you in future meetings also.

Barak Gaster: Excellent. Thank you. And so I think that brings us to… back to Chuck on update of existing formulary motions.

Chuck Agte: Yes and refining the formulary selection processes. So as I was eluding to earlier we have been engaging in further legal analysis on the… basically a very short set of rules in the Social Security Act that define how we can have a formulary and you guys have now, at this point, or at least some of you, we do have a member, have heard many times the key phrase that a lot of it comes down to is that we can only exclude products from the formulary; and when I say "we" I mean "you", because it's the prerogative of the board. We can only exclude products from the formulary when the excluded drug does not have a significant clinically meaningful therapeutic advantage in terms of safety, effectiveness or clinical outcomes of such treatment for such population over drugs included in the formulary and there is a written explanation of the basis of the exclusion.

Originally when we were going into the formulary development process, and this is new ground for everyone in terms of a state doing a

formulary under these guidelines. In that section that I just read we had originally had an interpretation of that that because the law says that the only time we can exclude a drug is when it is lacking that advantage that that was also the referred to basis for exclusion. That if that's the… if that was the only reason that we could exclude a drug, that that was also therefore the reason we were excluding it.

On further analysis, stakeholder input going back and forth with CMS for guidance on this, we have basically come to the conclusion that the basis for exclusion is more expansive than that. Essentially the lack of clinically meaningful therapeutic advantage is the threshold that allows us to exclude and then beyond that there is an actual basis for why we are excluding something that has met that threshold, which is also clear in your own deliberations as we've gone through the classes that we've reviewed so far. So for example with the angiotensin receptor blockers and this is where there's a significant difference in your role as the DUR board versus your role as the P&T Committee. When you're operating as the P&T Committee you're purely looking at the clinical aspects of the comparability of the drugs in the class. Whereas when you are working on the formulary in your role as the DUR Board you are making the selection based on all factors. And so for example with the angiotensin receptor blocker/direct [inaudible] inhibitor class when you reviewed it you established that you found the drugs to be primarily equal. We have, you know, without going into the details of the motion there are some drugs that were found to be more advantageous for certain conditions. You made your clinical decisions and then you moved on to looking at the cost and utilization information. And so in your actual deliberations once we selected what was being excluded you were in fact excluding on looking at the comparative cost of products in the class. And so that… in order to be able to accurately publish as required under the law the portion that says that there is a written explanation available to the public for the basis of the exclusion we need to kind of work on and refine the motions as we're moving forward to include what the board's actual basis for exclusion was. So beyond what your familiar with as your motions as the P&T Committee for the PDL where you essentially say, you know, you found the products to be equal, include or exclude this drug, beyond that all things are equal and then selection is left to the agencies. In this regard you have to make your clinical determination and then move on to the actual statement of, you know, based on

comparative costs of products in the class or if… in some cases like when we looked at the prenatal vitamins you looked at both comparative cost and you looked at volume of current utilization. So whatever factors you do in fact end up considering when we pick what will in fact be excluded, our motions need to document that as well so that we can publish the board's reason the specific products were excluded beyond the fact that they met the threshold to be eligible for exclusion on clinical consideration.

So that's where we are at in terms of why we are looking at refining the process. Because we do have to get to a point where the motions include those other considerations that you don't normally make as the P&T Committee.

Another factor that we'll be looking at for clarifications is, again, part of the difference between your role as P&T and your role as DUR is when you are acting as the P&T Committee on the PDL, again, you're essentially making a clearly clinical decision and often rendering a decision based on the chemical ingredient, not necessarily the brand or generic drug. You make your decisions based on the fact that, you know, pantoprazole or omeprazole or whatever the drug may be you're really just looking at what is the drug? Not, is it a brand? Is it a generic? What's available? Is brand or generic? Because you are making clinical decisions. With the formulary, again, because you're making the decision across the board we're going to need to get more detailed than we have been in what you're familiar with as P&T because for example in some of the past motions we have, again, referencing back to the angiotensin receptor blockers you made a motion where you cited a couple of drugs that should remain preferred for specific conditions. And we cited them by generic name. They're currently only available as brand name drugs. And so we would be looking for motions which clarify… now is the intent that a version of this product must be on the formulary? Must the brand name be on the formulary? Currently the brand is the only thing that exists. But that… we'll be looking for clarification of motions so that we have direction on… the drug must be included, but it could be the generic if a generic comes out. Because in the motions as is in some cases because they are citing only generic names as we're used to doing for the P&T. We don't have… although the board's intent was clear in the motion, which we have to work from to publish the board's

determination, in some cases it is… we may know or assume that, you know, when they said this they meant the generics whereas when they said that they meant the brands. We have to have more clarification of that in the actual motion in order to be able to not be making assumptions.

So that is kind of the basis for the reason that we're wanting to take a look at the motions again because we do need some refinement so that we can make a more accurate publication. Because based on the motions so far in the previous interpretation, right now our published basis for exclusion is merely the fact that the board determined that these products did not have a clinically meaningful therapeutic advantage over other drugs which were being left on the formulary.

That in and of itself is what we need to be able to flush out in our publications as the department in order to actually move forward with making them non-formulary. Beyond that we have to be able to publish that, you know, there was no significant advantage and based on costs the board is excluding this product over other less costly alternatives or however you as the board end up wording that. But we need that final piece of, you know, it met the threshold. Then what was the tipping point for why we're excluding things? Also the additional detail of whether we're including the brands intentionally, whether we're including brands until a generic alternative is available and getting into a little bit more of that detail. Do we have any questions before we ask you to start actually looking at the previous motions made so far? No? I talked too much already. Okay.

Barak Gaster: This is Barak Gaster. That was very good. Thank you, Chuck. Points well taken.

Donna, did you want to lead us through the updating of our existing motions?

Donna Sullivan: Sure. This is Donna Sullivan. So what I did is I had Leta pull up the table of indications for the angiotensin receptor blocker class and the direct renin inhibitors and unfortunately the table is on two pages. So the titles to all the columns are on the bottom of page 15 in your tab and the drugs are listed on page 16. So we will try to toggle back and forth as best we can. So bear with us as we go through this.

So I wanted to also draw your attention to the previous motion. The previous motion you really only focused on I believe two major indications. One was that the… for the treatment of hypertension and diabetic nephropathy was one of them and then you made a second motion looking at heart failure. So what I want to do is remind… really go through the motion. We tried to make an update to the template to make it a little bit more meaningful as Chuck was explaining about the brand and the generic products. We had done this before the AG gave us direction to give specific reasons why you removed certain products from the formulary. So what I wanted to do… and you have the monographs from the previous… for this drug class and I want to point out for any stakeholders that printed this or when you're looking through this, and I was surprised too, that it looks like things are blacked out in the monograph. Those were actually shaded yellow and so when they printed they came out black. So unfortunately it's not something secret, it's just that that information was highlighted yellow. If you need us to bring it up so you want to read it then we can. We have it on the computer. But I just wanted to bring that to your attention.

Christopher Smith: This is Christopher Smith, Donna. So why were those areas highlighted yellow? Is that because they were conclusions or particularly significant findings?

Donna Sullivan: I believe it was the newer information. That there were some safety indications that came out around the new direct renin inhibitor and MedImpact had inserted that information into the monograph. They had given us one monograph, if you remember, at one point in time, and then we cancelled that meeting or decided not to make formulary decisions at that meeting and we postponed it to the next meeting and during that time there was new safety information that came out that MedImpact put in and they highlighted it in yellow so that you would be able to see it. I can bring it up for you if you would like to see it.

Chuck Agte: And I'll note that the… the highlighted version if you look at it online for stakeholders then, you know, we have the information out there. Online you can read it in its highlighted form.

Donna Sullivan: Correct. Are you able to read that? I'll try to read it. So basically what it's saying is that April 2012 Novartis released a statement that it will stop manufacturing Valturna a single table containing aliskiren (a direct renin inhibitor) and Valsartan (an angiotensin receptor blocker). Novartis also updated the FDA label for Tekturna (aliskiren), Tekturna HCT, which is aliskiren and hydrochlorothiazide; Tekamlo, which is aliskiren and amlodipine; and Amturnide (aliskiren, amlodipine and hydrochlorothiazide) tablets to include the following information:

A contraindication against combined use of aliskiren-based products with ARBs or ACE inhibitors in patients with diabetes,

A warning against the use of aliskiren-based products in patients with moderate renal impairment, which is a eGFR <60 ml per minute who are also taking an angiotensin receptor blocker or ACE inhibitor.

This action was taken in response to the FDA's review of the preliminary ALTITUDE study data. In December 2011, after a median follow-up of about 27 months, the trial was terminated early for lack of efficacy. Higher risk of renal impairment, hypotension and hyperkalemia was observed in aliskiren compared to placebo treated patients. The risk of stroke (2.7% aliskiren vs. 2.0% placebo) and death (6.9% aliskiren vs. 6.4% placebo) were also numerically higher in aliskiren treated patients. So that is the highlighted information. I'll leave it up there. We do not have MedImpact on the phone for these monographs. So if you have questions, if you feel like you need more information then let us know and we can try to get that information back to you.

Okay. So the highlighted information here, the aliskiren in patients with diabetes treated with ARB or ACE inhibitor (ALTITUDE) study evaluated the effect of adding aliskiren 300 mg daily in patients with diabetes who also had renal disease and were on an ARB or ACE inhibitor. The primary efficacy outcome was at the time to the first event of the primary composite endpoint consisting of cardiovascular death, resuscitated sudden death, non-fatal myocardial infarction, non-fatal stroke, unplanned hospitalization for heart failure, onset of end stage renal disease, renal death and doubling of serum creatinine concentration from baseline and sustained for at least one month. The

trial was terminated early due to lack of efficacy after approximately 27 months of treatment.

This next one seems very similar to what I just read. So the aliskiren in patients with diabetes treated with ARB or ACE inhibitor (ALTITUDE) study evaluated the effect of adding aliskiren 300 mg daily in patients with diabetes who also had renal disease and were on an ARB or ACE inhibitor. The primary efficacy outcome was the time to the first event of the primary composite endpoint consisting of cardiovascular death, resuscitated sudden death, non-fatal myocardial infarction, non-fatal stroke, unplanned hospitalization for heart failure, onset of end stage renal disease, renal death and doubling of serum creatinine concentration from baseline and sustained for at least one month.

The trial was terminated early due to lack of efficacy after approximately 27 months of treatment. The investigators reported a higher risk of renal impairment, hypotension and hyperkalemia in patients receiving both aliskiren and an ACE inhibitor or an angiotensin receptor blocker compared to those patients receiving a placebo and an ACE inhibitor or ARB. The risk of stroke was 2.7% in aliskiren vs. 2.0% in the placebo and death was 6.9% in aliskiren vs. 6.4% in placebo. So the risk of stroke were also numerically higher in aliskiren treated patients.

And then the table it's just the incidence of selected adverse events in the ALTITUDE study. So the table at the bottom of page 13 is the adverse events that were presented in the ALTITUDE study.

The next highlight is on page 15 and it just reads aliskiren provides additional blood pressure lowering when used in combination with diuretics, and calcium channel blockers. However, concomitant use with ACE inhibitors or angiotensin receptor blockers is contraindicated in patients with diabetes. That's just reiterating the labeling update.

And the last highlighted is the highlighting of the drug in the table on page 17, which basically is just telling you that this product is no longer marketed.

So going back to our motions there are several… I wish we had two screens up here. Maybe the committee will want to pull their motion out of the binder so that you have it, but on… so that we can look at the indications and the drugs on one… in your handout and then we can read the motion on the screen as we go through.

The list of drugs was on page 16. Or those are the list of indications. We also have in your handouts the drug class… or the drugs within the class that you're looking at that had the drug utilization and that is in your binder as well. I had already pulled it out. So what we would like to do is… I don't know if you want to have a discussion or if you remember, you know, want to bring up… again, what you're looking at. The reasons why you made your decisions on which products you were going to exclude from the formulary. If you want to discuss that among yourselves or do you…

Barak Gaster: This is Barak Gaster. Thanks so much, Donna. I think that we do not need to re-discuss what we discussed before. I think that the state of motions that we made were fine for what was there. But I think that what we need to direct our attention to now is making additions to the motions to take into account the additional points that Chuck brought up this morning to clarify our… the reasons for our exclusion. And I guess… I think that's the main thing that I think we… I would suggest that we discuss now. Before we get there just the one thought that I had in reading these two motions again were that… so we have two submotions for the ARB class and the second one was for the specific indication of heart failure. I wonder if in the first one we should add an indication for that motion so that as the motion stands now it just says that I move that all drugs will be removed and I wonder if we would want to add the words I move for the indication of hypertension that all drugs are…

Susan Rowe: This is Susan Rowe. For that… for losartan actually we could add the diabetic nephropathy and the other indications.

Barak Gaster: Right. This is Barak Gaster again. I think… so here we are sort of re-treading the thought process that we went through before. So it may be that we left off… we failed to mention any indications because there were potentially so many.

Susan Rowe: So, in this motion if you look down at the bottom, you did actually have diabetic nephropathy in there, so let me just read the… it was after reviewing the clinical information for the drugs within the angiotensin receptor blockers and direct Renin inhibitors, drug classes and their combination products, I move that all drugs, except losartan and losartan/hydrochlorothiazide will be removed from the Washington Medicaid Formulary. No single drug or combination drug product in this class has a significant clinically-meaningful, therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment of hypertension and diabetic nephropathy for any subpopulation.

So you do have those indications in there, and so really what we had done in the new template is we say after reviewing clinical information for the drugs within the, you know, insert class, indicated for the treatment of medically accepted conditions, insert indications, so you would say hypertension, diabetic nephropathy. I move that no single brand or generic drug product in this class has a significant meaningful advantage… therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment of, restate indications.

Barak Gaster: This is Barak Gaster, so great. I think you have already identified this issue, so before we move on to the real meat of the motion revision, we need to get to… let's make sure that we at least are starting from a polished baseline, which would be this new template that we have, which better identifies what the conditions are that we are moving about.

Chuck Agte: This is Chuck Agte. I'd like to throw out there a couple of things for you. So, please note in the model language provided, for example with the ARBs here, this is kind of generic model language that staff have proposed for you guys to use. It's not always going to be 100% applicable to your decision on every class, because for example, if you look at this template, the template refers to basically the baseline of a class where we might be removing brands but leaving generics.

ARBs there are more generics coming out, so again it's… a difference would be like with the ARBs in your first motion there. You specifically cited two drugs and so that we don't potentially rehash it later to remind the board on the technicalities of… because we are

looking at the indications page there as well, you don't necessarily have to make a decision on every indication in the world. You can, if you choose to. If you don't choose to, so that you understand the outcomes there, when a drug has an indication the board has not made a specific ruling on, the drug will remain preferred for any indication that you have remained silent on. So, if drug X shares all the same indications as 30 other drugs in the class but it has one additional indication they don't have, you don't have to address that indication. If you don't address that indication that drug will remain preferred for any FDA indications that you have not commented on.

Donna Sullivan: So, really what we need is a statement… this is Donna Sullivan, saying we're removing these drugs because fill in the blank.

Barak Gaster: So, this is Barak Gaster, right. So, as Chuck was speaking earlier, the two points that it sounded like we especially needed to discuss were the question of including the consideration of cost in our motion and addressing the issue of the brand versus the generic, and it looks like in the template here we have a good suggestion for the wording for how to address the brand versus the generic issue so then the other important point for us to discuss is the wording that we would add to reflect the consideration of cost that we have certainly and appropriately used in our discussion and in our deliberation.

Susan Rowe: This is Susan Rowe. I have a quick question. So, in excluding drugs, is it… do we name the drugs we're excluding in the motion or in not naming them as a preferred agent for the formulary, is it assumed?

Chuck Agte: You can take either path, and I'm sure depending on the drug classes some will be more convenient, you know, if we're looking at a drug class that has five drugs in it and you're excluding three of them, it might be… when you're able to be more specific, more specific is better, but in a drug class like the angiotensin receptor blockers, there isn't a specific requirement to call it out drug by drug by drug. So, when you can, good. When it's not convenient, it's not a big deal. When you reference by exclusion… like, in your original motion for this class, it was fine to say we want to exclude everything, except losartan. For example, on the brand versus generic issue there that would be an example where some of the assumptions that we would have to make on your original motion for observation is you say, I

move that all drugs except losartan and losartan/hydrochlorothiazide will be removed from the Washington Medicaid Formulary. So, that would be a case where that… we do not have a clear direction in regard to that motion. The motion doesn't say generic for these products. So, in the theory, although we knew that you intended for the brand version of that to be excluded, that's an assumption on our part that's not indicated in the motion, for example.

Whereas then when we got to the congestive heart failure one, that's what made us realize that we can't make that assumption, because then in congestive heart failure you again referred to drugs by generic name that only exist right now as a brand. So, we would be on… on thin ice to say well in this motion we knew you meant only the generic, whereas in this motion we knew you meant that we're including the brands. So, we need to have that distinction within the motion itself.

Barak Gaster: So, this is Barak Gaster. So, I'm happy to take a stab at the wording of an additional statement to add to our motion if somebody is ready to transcribe my words. So, in light of their… so this would be at the end of the motion. In light of their clinical equivalence, and after review of the average cost and drug utilization data of the medications in this class, exclusions are made in favor of less-costly alternatives.

This is for the committee. So, we could either stop there – period, and I think that would be perfectly appropriate for this class. The additional wording that we may… we could use for this class as well, but especially for the prenatal vitamin class, would be… and so why don't you put in parenthesis this final phrase, with special attention to drug availability.

It's like I said. I think that final phrase was especially important when we reviewed the prenatal vitamin class that we wanted to make sure that we had some excellent input from members of the committee of how variable drug availability of various products can be at various times, and we wanted to be inclusive to make sure that there were several options available to both clinicians and pharmacists to get prescriptions filled. So I think we… that is certainly another consideration that we use from our drug utilization data in addition to cost. So, we could include that, and I think we certainly… we could try to remember to include that when we consider it or leave it as a

consideration for each motion, since we will at least think about it, even if we do not talk about it out loud.

Donna Sullivan: This is Donna Sullivan. I'm just adding back in the fact that you wanted valsartan and valsartan/hydrochlorothiazide to be on…

Chuck Agte: Losartan.

Donna Sullivan: …the preferred drug… and losartan, losartan/hydrochlorothiazide, because as it reads right now you're removing… all of the brands would still be on the formulary, except for the Cozaar and Hyzaar or the products that have generic equivalent. So, anyway, let me just finish typing real quick, and then I'll show you what I did.

Chuck Agate: Donna, while you're redoing some of this, I think for this particular class we need to avoid the use of word multisource as it appears higher in there, because many of the drugs the board was planning to exclude or actually single-source still unbranded.

Christine Klingel: This is Christine Klingel. As you're typing, Donna, do we need to have the generic products listed if we say that a brand name product shall be excluded from the formulary when its generic becomes available? Because even right now, I think valsartan just became generic, and I believe candesartan is supposed to go generic the end of this year. So, we had talked about if we say that they can go on the formulary once they're generic, but then we say that all of them except losartan is available now.

Donna Sullivan: This is Donna Sullivan. The statement that is saying a branded product shall be excluded from the formulary when its generic equivalent becomes available is really for when you make a drug selection where the only available option is a brand, but then sometime before you review the class it becomes generic, that we're able to switch to the generic product, as the formulary item, and remove the brand from the formulary. So, that is really just kind of a blanket statement for when we have those types of situations occur. So, if you want to… at this time, I feel like you should just really clarify the reason why we're making the motion that you made and maybe not necessarily change the drugs that you're adding or removing from the motion.

Chuck Agte: And it would depend on the boards intent and that's why I was kind of talking about the template versus what you've done with any particular class, because for example, in your original motion and from the minutes of that meeting, it was clear that your intent at the last meeting for the non heart failure indications was that you were specifically keeping losartan and its HCTZ combo. So, depending on how you word the motion would determine did you really mean that moving forward, generic losartan and losartan/HCTZ are the formulary drug for those conditions, or did you also mean depending… and that's why we need to look at how we fine tune this is, if you just word it as the brands are being removed, we could… sorry. I'm trying to figure out how to say this out loud and I'm thinking faster than I'm talking.

Is it your intent that those two generic products be the ones that are preferred formulary, or is it your intent that as other generics come out, the other generics could also be formulary? So, that would be kind of a line that, like I said, from your first review of this class it appeared that you were saying you wanted losartan and losartan/HCTZ specifically, and so we need to be careful in the wording so as to be able to make the distinction between when you're calling out specific generics, that these are the preferred formulary products, or when you're saying that these are the ones, based on what's generic today, we'd allow other generics later. So, that's another distinction to keep in mind when you're fine-tuning the wording.

Christopher Smith: This is Christopher Smith. We're calling out losartan, I believe, and losartan/hydrochlorothiazide because we have had the opportunity to review their comparative costs and drug utilization, and I think we don't have the evidence… we don't have that information about those other generics. It's not available. So, I don't think we could act on that.

Susan Rowe: This is Susan Rowe, and I would add to that, that as Donna's doctoring our statement to include the congestive heart failure, that specifically we did look at evidence and clinical evidence. So, that's the inclusion there.

Chuck Agte: Exactly. I wasn't suggesting you change your decision.

Barak Gaster: This is Barak Gaster. We appreciate your looking out for us, Chuck, and I think that we should stick with what we've got and that the future vaguerities of additional generics and how they may be priced and how they might be utilized is too complicated for us to try to predict, and we should stick with the list of preferred products that we've got. So, I think we just need to read through this again and make sure that we're good. If you could scroll down a little so I could see the bottom of it.

What I especially want the committee to help me with is this last very long sentence that I've added, which I think certainly could use some wordsmithing if we feel appropriate.

Donna Sullivan: This is Donna Sullivan. Can you clarify kind of what your intent was with the last parenthetical statement?

Barak Gaster: Yeah.

Donna Sullivan: With special attention to drug availability.

Barak Gaster: Right. This is Barak Gaster. I think that now that we have changed the wording a little bit that the third to the last line, I think you might be able to take out exclusions are made. Just leave it right there for a second. Let me just read it again. Yeah. You're right.

Donna Sullivan: I think you could take it out.

Barak Gaster: Yeah. We'll take it out. So, now that it says up above that we're… yeah.

Susan Rowe: Uh, Donna… this is Susan Rowe. What Barak was talking about with the parenthetical statement is it will be really very important when we… not for this class but the prenatal vitamins. That was part of the discussion.

Donna Sullivan: Okay.

Barak Gaster: This is Barak Gaster. In addition to… there were two types of drug utilization data that we reviewed. One was average cost but the other was which products were being used in this, and then we had very

important input from committee members about how drug availability disruptions can really affect a specific drug class. So, that was also a consideration that we made in addition to the costs, but I think… I wrote that as I was sort of thinking about what this clause in our motion would look like. I was thinking about it across various drug classes, not just this one, and I think that we could leave out that parenthetical statement for the ARBs, since I don't think that there are any problems with drug availability with any of the drugs that we've reviewed in this class. I think we are maybe ready to make this motion.

I want to take a moment to just check to see if there are any stakeholders who have comments before we make this motion and vote on it.

Woman: There is no one signed in.

Barak Gaster: Okay.

Chuck Agte: This is Chuck Agte. I would actually like to ask a couple of questions on the motion. Even before we get towards making it more official, towards the middle of the motion they say the branded products within the class do not have significant meaningful therapeutic clinical advantage over the generic equivalence, in this particular class, most of the drugs we're talking about don't have generic equivalence. We're not actually comparing them to their generic equivalence.

Donna Sullivan: I believe this… this is Donna Sullivan. This would be a statement that is basically saying Cozaar and Hyzaar are not more effective or provide more advantage over the generic losartan and that it's specifically stating that the brand will be removed from the formulary, and to me, the next sentence is not necessary.

Barak Gaster: This is Barak Gaster. I agree with that, and why don't we take that next sentence out. Thank you.

This is Barak Gaster, and that gets us to one screen too. So, any other comments or suggestions from the committee about this motion? I will go ahead and make this motion. After reviewing the clinical information for the drugs within the angiotensin receptor blockers and

direct Renin inhibitors class indicated for the treatment of the medically-accepted conditions hypertension and diabetic nephropathy, I move that no single brand or generic drug product in this class has a significant clinically meaningful therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment of hypertension and diabetic nephropathy for any subpopulation. The branded products within the class do not have a significant meaningful clinical advantage over their generic equivalents and are excluded from the formulary. In light of their clinical equivalents and after review of the average cost and drug utilization data of the medications in this class, all drugs except generic losartan and generic losartan/hydrochlorothiazide shall be removed from the formulary in favor of less-costly alternatives.

Christopher Smith: This is Christopher Smith. I second.

Barak Gaster: All in favor say, aye.

Group: Aye.

Barak Gaster: All opposed, same sign. So, that motion passes.

Donna Sullivan: Okay, so this is Donna Sullivan. So, the next motion that you passed was for heart failure, so I'm going to replace the indications of hypertension and diabetic nephropathy with heart failure, and I will add the valsartan and valsartan/hydrochlorothiazide.

Chuck Agte: And candesartan, as well.

Donna Sullivan: Okay. I've finished it.

Barak Gaster: This is Barak Gaster, and on the fifth line I think you can change conditions to condition.

Eric Harvey: This is Eric Harvey. I think this motion we really need to highlight that these three medications do have a clinical advantage, and that's why we're calling them out and so it's not the same form of a motion as the previous motion.

Donna Sullivan: Okay. So, what… in the previous motion… this is Donna Sullivan. The board finds that valsartan, candesartan, and the combination products have a significant clinically meaningful advantage in terms of safety and efficacy. If you'd like, I can copy and paste that in here? Okay.

Susan Rowe: This is Susan Rowe. I agree with Eric; however, we are calling them out because they have a significant advantage. However, I would like to put the provision in there that a generic may be used in the future when it's available or that when the generic is available, the branded would then be excluded.

Christopher Smith: This is Christopher Smith, and I wonder whether we are then making an assumption that based on comparative costs, historical generics are cheaper, but we don't have that data specifically, and whether or not that's an issue and then if we could have such a proactive determination without having all the facts upon which to make that decision.

Donna Sullivan: This is Donna Sullivan. I think you could go ahead… I don't think you have to say that the drug that you have reviewed the cost on all these products and that you have determined that one is less costly but equally effective. I think that you could put the least costly equivalent product, or you could just say when it becomes generically equivalent and more cost effective, the brand shall be removed.

So, what I did is I… this is Donna Sullivan. I inserted the statement from the previous motion, the board finds that valsartan and candesartan and their combination products have a significant clinically meaningful therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment of heart failure for any subpopulation. So, then we're back to the… no single brand or generic product in the class has… I'm going to remove this statement. My thinking… is that accurate?

Woman: Yeah.

Barak Gaster: This is Barak Gaster. Yes.

Donna Sullivan: Okay. And so then we're back to the branded products within the class do not have a significant meaningful clinical advantage over their generic equivalents and are excluded. We can re-insert the statement that we took out of the previous motion where… and I forget what exactly it said, hang on. That stated a branded product shall be excluded from the formulary when its generic equivalent becomes available. I can put that back in there. Okay.

Christopher Smith: This is Christopher Smith. Do we need to specify why we would be making that determination based upon anticipated cost advantage?

Barak Gaster: This is Barak Gaster. I think that would be fine. So, after available due to anticipated cost advantage.

Eric Harvey: This is Eric Harvey. Can you scroll up a little bit on that? Should we not specify that combinations are the hydrochlorothiazide combinations, because there are other combinations that we are excluding?

Christopher Smith: This is Christopher Smith. Eric, are you referring to the amlodipine…

Eric Harvey: No.

Christopher Smith: …combinations? And did we see any data on that? I don't remember reviewing those combinations. Maybe they're not part of this drug class, because they include another drug class?

Donna Sullivan: This is Donna Sullivan. We had included… we had reviewed those kind of as an addendum to the actual monograph. What I'm doing is I'm taking… I'm copying candesartan/hydrochlorothiazide, and valsartan/hydrochlorothiazide and we'll specifically call those out instead of just relying on combination.

Christopher Smith: This is Christopher Smith. So, then what is the status of the ARB/amlodipine combinations?

Donna Sullivan: They are removed. Based on what you said here, all drugs… these are the only ones that are formulary, so the other ones would be nonformulary.

Christopher Smith: So, this is Christopher Smith. As a prescriber then, if someone wanted those drugs, they would just prescribe them independently, the amlodipine.

Donna Sullivan: If they could, yes.

Christopher Smith: Okay. That makes sense.

Deb Wiser: This is Deb Wiser. Could you scroll down a little bit, too, on that sentence that started with a brand name? A branded product, should that say not listed above? Oh no, that wasn't it.

Barak Gaster: No, I think…

Deb Wiser: No, that one's okay.

Barak Gaster: This is good.

Deb Wiser: It's the sentence before that. The branded products within the class do not have a significant meaningful advantage, but we are listing branded products above that. We're saying do, so I would think the branded products not listed above within the class would be more accurate.

Donna Sullivan: This is Donna Sullivan. Previously, we said the multisource branded products within the class do not have… what you're trying to say is that the brands are no more effective than their generic equivalence, and at this time, these products I don't believe have generic equivalence.

Christine Klingel: This is Christine Klingel. Actually, valsartan just did and candesartan will probably by the time this becomes effective.

Deb Wiser: Okay.

Donna Sullivan: So, that point might be null, but it's fine to have it in there.

Eric Harvey: This is Eric Harvey. On the next sentence where it says a branded product shall be excluded from the formulary when the generic equivalent becomes available, should we say may instead of shall?

Chuck Agte: This is Chuck Agte. No, because as the board you are the decision makers. You cannot delegate to us and say that we may do it in absent of your decision. So, either we shall do it when it happens based on your direction or we will do something else based on your direction, but it needs to be a specific direction rather than permissive language.

Eric Harvey: This is Eric Harvey. Thank you for the clarification.

Barak Gaster: Another bit of wordsmithing, if we're ready for another puzzle, but the earlier sentence ends with 'for any subpopulation,' and I think that came from when we had a negative statement when we said that a certain drug did not have an advantage for any subpopulation. I just wonder whether this is… I think the intent is clear, but does that read logically to you if you say that…

Chuck Agte: This is Chuck Agte. So, for clarification in case it needs wordsmithing rather than deletion, the federal language that we are trying to be compliant with deal with drugs for specific indications is usually what we've been talking about to shorthand it. Technically, it's drugs for a specific indication for any given subpopulation. So, there are times when we've called out for any subpopulation to make it clear that you are finding there is or isn't an advantage for everyone. As yet, we have not run across drugs that you say find a certain age, racial group, gender, demographic where one drug might be better than another. So, that hasn't really come up, and we've been generalizing by saying for any subpopulation so it's clear that you were not accidentally silent on some populations that may need to be called out.

Barak Gaster: All right. This is Barak Gaster. I want to keep us moving along. I think we are probably at a good spot with the wording of this motion. So, is there anyone who would like to make this motion?

Mason Bowman: Mason Bowman. I'll go ahead and do it. After reviewing the clinical information for the drugs within the angiotensin receptor blockers and direct Renin inhibitors class indicated for the treatment of the medically-accepted condition of heart failure, the board finds that valsartan, valsartan/hydrochlorothiazide, candesartan, candesartan/ hydrochlorothiazide have a significant clinically meaningful therapeutic advantage in terms of safety, efficacy or clinical outcome

for the treatment of heart failure for all populations. The branded products within the class do not have a significant meaningful clinical advantage over their generic equivalents, and are excluded from the formulary. A branded product shall be excluded from the formulary when its generic equivalent becomes availability due to anticipated cost advantage. In light of their clinical equivalence and after review of the average cost and drug utilization data of the medications in this class, all drugs except generic losartan, generic losartan/hydrochlorothiazide, valsartan, valsartan/ hydrochlorothiazide, candesartan, and candesartan/ hydrochlorothiazide shall be removed from the formulary in favor of less costly alternatives.

Christopher Smith: There is just one type-o that I heard. This is Christopher Smith. The first sentence is even longer. So, go all the way up, Donna. Mason Bowman read it without a pause there. So, a comma after the word heart failure, right there, yeah, and that continues on.

Donna Sullivan: This is Donna Sullivan. So, make this one complete sentence?

Christopher Smith: Correct.

Donna Sullivan: Okay.

Christopher Smith: That's how it reads. And then just remove the capital T there. This is Christopher Smith. I second.

Barak Gaster: All in favor say, aye.

Group: Aye.

Barak Gaster: All opposed same sign. So, that motion passes, as well. All right.

This is Barak Gaster. So, we are going to now turn our attention to the prenatal vitamins, and we are going to need some copy and pasting down from the hard work we just put in on the ARB class to review our motion on the prenatal vitamin class.

This is Barak Gaster. I think we spent a lot of time on this class, and I think we did some very clear thinking and deliberating, all of which I think still stands, and I think that we can probably do a quick revision.

Deb Wiser: This is Deb Wiser. I am just trying to remember… I see it on our prior statement that we had chosen prenatal plus, and I cannot remember whether we were including DHA formulations with and without iron by stating just prenatal plus?

Chuck Agte: This is Chuck Agte. Having recently reviewed the minutes of this meeting, my impression of that is that you were specifically calling out prenatal plus. Any product under that branded name due to the fact that the majority of our… not the majority but a large portion of the utilization was already in that product implying that it was a product commonly available and commonly used by pharmacies. So, I believe it was more a decision based on utilization and presumed availability based on that utilization and that the prenatal plus was being called out regardless of form or content, as anything labeled prenatal plus.

Deb Wiser: Deb Wiser. Thanks.

Donna Sullivan: This is Donna Sullivan. There are generic products within the DHA prenatal vitamin subclass. So, this motion just removed the branded products and left any generic product regardless of if it was DHA or non-DHA on the formulary.

Barak Gaster: This is Barak Gaster. I bring this up with some hesitation but yesterday I was having difficulty prescribing oral contraceptive and the issue was that it was a branded generic oral contraceptive. Is that… I mean, does that make all of this more complicated?

Donna Sullivan: Yes. Prenatal plus… this is Donna Sullivan. Prenatal plus is, I believe, a branded generic also, and if you look at the cost of it, it's like eight cents per tablet and that was another reason why there's a large utilization and why you called it out specifically.

Barak Gaster: Okay.

Chuck Agte: And for the sake of transparency, in the listings that you guys have for the prenatal vitamins that you are looking at for cost, etc. The normal

distinction for prescription products of brand and generic is less clear in vitamins, because they don't go through the same sorts of approval process, and the actual distinction on brand and generic within this class of products was based on whether or not they had a copyrighted or trademarked name that was used on the product or whether they had not copyrighted or trademarked that, because every single version of product is considered its own independent version. They all put a name on it. The distinction of brand and generic came from whether it was a trademarked name or not.

Barak Gaster: All right. This is Barak Gaster. I think for this class, let's go ahead and add in the parenthetical clause that I had mentioned for the previous class we left out before. So it's in light of the clinical equivalence and after review of the average cost and drug utilization data of the medications in this class, with special attention to drug availability.

Donna Sullivan: This is Donna Sullivan. Do you want it at the end where it was before? I think I lost you there.

Barak Gaster: Okay. Let me go back. So, in light of their clinical equivalence and after review of the average cost and drug utilization data of the medications in this class, with special attention to drug availability, great. I want you to take out the comma, the last comma of that sentence that you were just on. So the third to the last line after formulary no comma there. Good. So, let's remove this next paragraph.

Donna Sullivan: This is the...

Barak Gaster: All right. Now, it's…

Donna Sullivan: This is Donna Sullivan. So, never mind. I answered my own question.

Barak Gaster: Yeah, if you could scroll up and let's just read this.

Christopher Smith: This is Christopher Smith. The intent of the comment about… for the medically-accepted condition, we need to specify why we're making this formulary recommendation. We have to have a specific condition.

In light of that then, by defining pregnant women, do we limit this to women who are pregnant?

Donna Sullivan: Yes.

Christopher Smith: Women who are intending pregnancy or women of childbearing age or other potential indications? Do we need to be very specific about that?

Deb Wiser: This is Deb Wiser. This is actually an issue, because the need for folic acid supplementation prior to becoming pregnant is important in preventing neural tube defects.

Donna Sullivan: This is Donna Sullivan. I was just copying and pasting what you had put in the previous motion. So, that is up to you.

Barak Gaster: This is Barak Gaster. So, as good as we thought it was before, we're going to make it even better. So… but right, we need to figure out exactly how we're going to state that.

Donna Sullivan: This is Donna Sullivan. I have a question for Chuck. Do we cover prenatal vitamins in those instances, or do we only cover them once the pregnancy is confirmed? I would ask that.

Chuck Agte: There is a slight difference between our current clinical policy intent and what is supported in claim editing. So, the previous policy intent by the agency was that we cover prenatal vitamins for pregnant women, but if the board gives us direction otherwise, we will happily follow other direction. At this point in time, our policy is we cover prenatal vitamins for pregnant women and/or women who are breastfeeding. The actual application of that at this time is that we limit coverage to women between the age of 10 and 40. We exclude coverage for males. We don't really have a pregnancy indicator in our system, so we have it limited to women of childbearing age and if you are outside of that age range, it requires prior authorization and at that point we would verify whether or not the client was pregnant. So, if we got a request for a 42-year-old woman and we verified pregnancy, we would go ahead and approve. At this point in time, outside that age range is the only time we would looked at it, and if the board would like us to consider things other than pregnancy, we would request that direction.

Barak Gaster: This is Barak Gaster. So, I think we can look at the wording here and say… make that wording fit the current usage. So, after reviewing the clinical information for the drugs within the prenatal class indicated for the treatment of the medically accepted condition, vitamin supplementation in women of childbearing age. Is that a medically-accepted condition?

Woman: Yes.

Barak Gaster: Excellent.

Deb Wiser: This is Deb Wiser. Childbearing is one word, I believe.

Barak Gaster: Actually, do we want to say that… anything else? I believe it's perfect the way it is… childbearing age.

Donna Sullivan: This is Donna Sullivan, and I'm sorry I interrupted you, but if you leave it as just women of childbearing age, then we cover it for any woman for any reason that is within childbearing age.

Barak Gaster: This is Barak Gaster. Because I think it… we do not want to be in the business of trying to figure out whose intending a pregnancy and who's not intending a pregnancy. I think…

Donna Sullivan: This is Donna. I realize, okay, I'm just trying to say that then if you… any doctor then could prescribe a prenatal vitamin to a woman in lieu of a multivitamin that is not covered for multivitamin supplementation just as a daily supplement with no intention of ever having a child.

Deb Wiser: This is Deb Wiser. You could clarify it by saying women of childbearing age with the possibility of pregnancy.

Chuck Agte: Well, that's… this is Chuck Agte. That is, in fact, any woman of childbearing age.

Deb Wiser: Well, not exactly.

Donna Sullivan: With the intention of pregnancy, maybe.

Barak Gaster: Okay. That sounds good. I think that's fine. So, this Barak Gaster. Accepted condition vitamin supplementation in women of childbearing age who are planning to be… or…

Deb Wiser: Intention of pregnancy.

Barak Gaster: Yeah, but I don't know if it… maybe not intention. I mean…

Christine Klingel: This is Christine Klingel. I don't think we need to put that in there at all. I mean, there are so many accidental pregnancies, I think I would much rather pay eight cents a tablet and have a 13-year-old on a prenatal vitamin just in case than try to split hairs. It would be so hard to enforce that, yeah.

Barak Gaster: Yeah, this is Barak Gaster. I agree with that, and I go back to my previous consideration to try to identify who is intending pregnancy, who may be getting pregnant, who will definitely… I mean, I think we would want to cover this in just about all women of childbearing age, unless they have an extremely rare situation in which they do not have any possibility of becoming pregnant, which is a pretty small group of people. So, I would say let's leave that off and leave it be women of childbearing age.

Donna Sullivan: This is Donna Sullivan. I just want to push back. So, we could say who are pregnant or intending to get pregnant. An accidental pregnancy is not intended, but then you wouldn't know you're pregnant until you go to the doctor and find out that you are pregnant. So, I'm just pushing back. The other thing, too, is, you know, with childbearing age, if the intention is to treat anybody that might becoming pregnant, you know the age of 40 is, you know, not necessarily as… most women over the age of 40 are still of childbearing age and still could become pregnant. So, I'm trying just to decide what we should be putting in there.

Christopher Smith: This is Christopher Smith. I think that we don't, as physicians, usually distinguish when we recommend a prenatal vitamin. We say you're a young woman, it's a good idea to take one. There are some situations where a woman might say, but I don't think I'll get pregnant, and then that's fine. They can make that their own personal choice, but I generally, as a physician, do encourage women to take a prenatal

vitamin when they're of childbearing age, and I agree that could extend up to age 45, potentially later if they're doing extravagant medical therapy to get pregnant. So, I don't know how you would define it as a pharmacist if you see such a patient, but I think that just to define it as childbearing age, that's the medical condition that we're talking about.

Donna Sullivan: Okay.

Barak Gaster: This is Barak Gaster. I mean, we could add… if we added the words vitamin supplementation in women of childbearing age who might become pregnant.

Deb Wiser: This is Deb Wiser. I think that is a better way to narrow it down slightly.

Barak Gaster: So, I mean, so then we're… it sounds less blanket. We are… if somebody has had a hysterectomy, we are not going to cover it, and I think that sounds good to me. So, let's read this again.

So, this is Barak Gaster. We've got another usage of the medical indication terminology on the sixth or seventh line for the treatment… okay, so it's like outcome for. So, let's go up to… so start at the treatment with the one line above that. So, I think it would be outcome for, so back the cursor up. No, I think we want to take the treatment outcome for…

Donna Sullivan: I was just gonna put it as…

Barak Gaster: Yeah, great. Perfect. If you could scroll.

Donna Sullivan: This is Donna Sullivan. Do we need to say medically accepted condition, Chuck? Or can we just say for the vitamin supplementation of women?

Chuck Agte: I think we can get rid of that part. The reason that it got incorporated into the template language was when we were potentially dealing with a drug class where there's half a dozen drugs, and they all have half a dozen shared medically accepted indications or when you're trying to rule generally on something where four out of five products when we say medically accepted that restricts. If you have accidentally said

these six products are all good for something, it allows us to further limit.

Donna Sullivan: Okay. Great. Would you like me to delete that?

Barak Gaster: So, this is Barak Gaster. Please delete that. Could you scroll down, please? Great.

This is Barak Gaster. That looks pretty darn good, even better than it was before.

Chuck Agte: Chuck Agte. I apologize. As written, your statement relates to… we have now accidentally refined it only to women who might become pregnant, which is excluding women who actually are.

Barak Gaster: This is Barak Gaster. Thank you. So, you're right. So, it's who are or might become pregnant or who are breastfeeding.

Deb Wiser: This is Deb Wiser. If breastfeeding is inherent in might become pregnant.

Barak Gaster: Great. Perfect. Anything else from anybody? This is Barak Gaster. Great. I will read this motion. After reviewing the clinical information for the drugs within the prenatal vitamin class indicated for the vitamin supplementation in women of childbearing age who are or might become pregnant, I move that no single brand of generic drug product in this class has a significant clinically-meaningful therapeutic advantage in terms of safety, efficacy, or clinical outcome for vitamin supplementation in women of childbearing age who are or might become pregnant. The brand of products within the class do not have a significant meaningful-clinical advantage over their generic equivalents and are excluded from the formulary in light of their clinical equivalence, and after review of the average cost and drug utilization data of the medications in this class with special attention to drug availability, all brand drugs, except prenatal plus, shall be removed from the formulary in favor of less costly alternatives. Women will not be required to change to a formulary product during a course of therapy.

Mason Bowman: Mason Bowman. I second.

Barak Gaster: All in favor say, aye.

Group: Aye.

Barak Gaster: All opposed same sign. And that motion passes. All right, we are going to take a short break, and we are going to reconvene in exactly 12 minutes at five minutes before 11:00. Thank you.

All right, we are going to reconvene now if everybody could please take their seats. This is Barak Gaster. We will now be doing a drug class review of the bone density regulators for osteoporosis, and we have ODS MedImpact on the line who will give us a presentation of their monograph.

Kevin Leung: Thank you. This is Kevin from MedImpact, and I will proceed with the presentation. Today, we will be reviewing the osteoporosis category specifically to evaluate the clinical efficacy and safety evidence for the pharmacologic agents for osteoporosis with a focus on the oral and IV bisphosphonates and the RANKL inhibitor monoclonal antibodies.

Osteoporosis is a skeletal disorder characterized by low bone mass and micro-architectural deterioration of bone tissue with consequent increase in the fragility of bone and increased risk and susceptibility to fractures. It is defined as having a bone mineral density of more than 2.5 standard deviations below the mean. An estimated 10 million Americans…

Barak Gaster: Are you on the line still?

Regina Chacon: Hello, anybody there?

Kevin Leung: Hello.

Regina Chacon: Hi. This is Regina in the meeting. I'm sorry. We lost our connection.

Kevin Leung: Sorry. For some reason I got disconnected. All right. That's the reason I got disconnected. Okay, so I am moving onto the second slide.

Barak Gaster: And this is Barak Gaster. If you could please… jus reminding you to let us know when you're going to the next slide so we can advance the slides here.

Kevin Leung: Sounds good.

Barak Gaster: Great. Thank you.

Kevin Leung: Okay. No problem. Now, going on to slide two, bone is a dynamic tissue constantly influx between resorption and formation. These processes are carried out by osteoclasts and osteoblasts along with osteocytes, which are internalized osteoblasts that help maintain bone tissue. The pharmacologic coproducts listed below work on either the bone maintaining process or the bone building process. The pharmacologic measures can be divided in two different categories, bone maintaining and bone building. Regardless of the medications the member will be using, the National Osteoporosis Foundation recommends adequate amounts of vitamin D and calcium along with appropriate lifestyle modification for all individuals aged 50 or older.

Starting with bisphosphonates, they are a nonhormonal agent that decreased bone resorption by attenuating osteoclast activity. Bisphosphonates have a higher affinity to [inaudible] at site of active bone resorption where the drug is taken up by osteoclasts. A nitrogen containing bisphosphonate block critical pathways for osteoclast cell form and function leading to programmed cell death or [inaudible].

All bisphosphonates act similarly. However, their binding affinity and antiresorptive potency differs amongst bisphosphonates. In accordance to binding affinity, zoledronic acid has a greater binding affinity than alendronate to risedronate. With a higher binding affinity, zoledronate, for example, will allow for less frequent administration needs compared to risedronate. Alendronic acid, brand name Reclast, is dosed IV once a year. However, oral products, such as risedronate and alendronate are dosed.

With the exception of previously-mentioned differences in binding affinity, relatively similar outcomes in surrogate markers and clinical end points were demonstrated in meta analysis. There is a new

medication – [inaudible] is a new formulation of alendronate that was FDA approved in August of 2012. The difference is that it is an oral solution that is buffered to a pH of 4.8 to 5.4 to provide better alendronate absorption and potentially reduce the risk of developing gastrointestinal lesions. However, similar to Fosamax, [inaudible] is recommended that a patient wait at least 30 minutes before the first food, beverage, or medication of the day and also before lying down.

Moving to the RANKL inhibitor antibodies, denosumab, is the latest FDA product that was approved, indicated for osteoporosis in postmenopausal women at high risk for fractures. Since RANKL inhibitors is a new novel therapy, we will discuss this more in detail in a later section.

Now moving to selective estrogen agonist antagonists, these agents have estrogen agonist activity in the bone tissues, and they oppose the action of estrogen and other tissues. With [inaudible] to polypeptide hormones, calcitonin is a peptide derived from the perifollicular cells of the thyroid and is a direct inhibitor of osteoclast activity. It is available in both injectable and nasal spray formulations. The nasal spray is the most commonly used.

Finally, from the bone maintaining category, estrogen serves as an antiresorptive agent and inhibits bone resumption, increased bone mineral density, and reduces the risk for both vertebral and hip fractures. While conjugated equine estrogen has positive effects on bone in the WHI study, the effect was overshadowed with an increase in cardiovascular events, dementia, gallbladder disease, and breast cancer. The current recommendations support the use of low-dose estrogen replacement for menopausal symptoms and only to be considered as agents to be used solely for the prevention of osteoporosis therapies when non-estrogen based therapies cannot be utilized.

In the right panel with the bone building category, teriparatide is a 134 end terminal fragment of human parathyroid hormone and appears to contain all the anabolic properties of a full length parathyroid hormone. Unlike resorptive agents that inhibit bone resumption and preserve bone architecture, teriparatide stimulates osteoblastic

activities and new bone tissue from its formation. Current consensus places this therapy as an option for those that failed other therapies.

Moving on to slide three, the FDA approved osteoporosis indications. These indications can be differentiated for postmenopausal versus glucocorticoid-induced osteoporosis. Postmenopausal osteoporosis is associated with estrogen deficiency, which increases the skeleton sensitivity to parathyroid hormone, which in turn increases calcium resorption for the bone. Glucocorticoid-induced osteoporosis results from the presence of other diseases or conditions that can [inaudible] both patients to bone loss, such as genetic disorders and hypogonadal state, such as Turner syndrome.

Products can be further broken down for prevention versus the treatment of osteoporosis. Of relevance, Prolia has been recently approved in 2010 for the treatment of osteoporosis and there have been some new generic approvals starting in 2008 with calcitonin and alendronate and more recently in March 2012 with ibandronate and moving forward in the future, Reclast will be generically released in March 2013.

Moving forward to slide four, comparing the efficacy of these various products, admittedly there is a paucity in research comparing the product with head-to-head trials. However, when we look at the risk reduction of all these products compared against placebo, the risk reductions are vertebral fractures have been demonstrated to be very similar, and in the second part of that section, looking at the comparative efficacy, risk reductions of other fracture sites, there is a similarity in risk reductions with vertebral fractures showing that zoledronic acid and teriparatide has a 60% risk reduction similarly with the alendronate, risedronate, and ibandronate at 50%.

The nonvertebral fractures do slightly vary with teriparatide at 50% risk reduction and risedronate and alendronate sharing a 20-25% risk reduction on nonvertebral fractures, and the most common, hip fractures, alendronate has a 50% risk reduction.

Moving on to slide five. Now, we look at the new therapy… the new novel therapy, denosumab. It's FDA approved for the treatment of osteoporosis in postmenopausal women at a high risk for fracture, and

of note, it is the first biologic treatment for osteoporosis utilizing full human monoclonal antibodies to RANKL, which stands for receptor activator of nuclear factor K-like chain enhancer of activated D cells. It is still 60 mg subcutaneously every six months, and at the time of the initial presentation, the manufacturer was seeking subsequent FDA approval and more recently in September 2011, they received approval for the reduction of skeletal-related events in patients with bone metastases for prostate cancer.

Moving on to slide six. This shows how this new RANKL inhibitor works, and if you look on the top right hand of the slide, you will see a molecule of denosumab, and it binds to RANKL which expresses the transmembrane encroaching by osteoclasts and their precursors, which is essential for the formulation and function and survival of osteoclasts. The findings to RANKL prevent the activation of the receptor, RANK, on the surface of osteoclasts and their precursors, thereby inhibiting osteoclast formation, function, and survival resulting in decreased both presumption and bone loss.

Going forward to slide seven, looking at the clinical efficacy, in evaluating the clinical efficacy, a three-year randomized double-blind placebo-controlled trial, the Freedom Trial, fracture reduction evaluation of denosumab in osteoporosis every six months enrolled 7,800 postmenopausal women, ages 60-91. Denosumab was associated with lower incidents of vertebral, nonvertebral and hip fractures in women with osteoporosis. The drug was administered as a 60 mg subcutaneous injection every six months versus placebo at three years. The trial resulted in 68% reduction in vertebral fractures, 40% in hip fractures, 20% in nonvertebral fracture, and a significant increase in bone density at the lumbar spine, total hip, and femoral neck.

Comparing denosumab versus alendronate, the Decide Trial was a one-year double-blind noninferiority trial that demonstrated a greater increase in bone mineral density with denosumab than alendronate at all skeletal sites. The Stand Study also demonstrated similar benefits. It showed significant greater increase in bone mineral density resulting at the total hip, lumbar spine, and distal radius in women who switched to denosumab than in those who continued alendronate after one year.

Barak Gaster: This is Barak Gaster. Can I ask you a quick question about this slide?

Kevin Leung: Yes.

Barak Gaster: So, I'm just having trouble understanding… I understand there is a significantly greater increase in bone mineral density but without those numbers, I can't really tell whether that's a clinically significant difference or just a statistically significant difference. Do you have those numbers handy?

Kevin Leung: I don't have them right now, but I can get the information. What are you specifically looking into, the differences between both products?

Barak Gaster: Right. Understanding the difference between the denosumab and the alendronate in the Decide Trial. It's not helpful for us to just know that it was a significantly greater increase without knowing what the absolute difference was to understand if this was a clinically significant difference or just a statistically significant difference.

Kevin Leung: Okay. Let me… I can pull the trial immediately after the presentation and depending on how much time I have, I can site those numbers during this meeting.

Barak Gaster: Thank you.

Katie: Kevin, this Katie with ODS. I just wanted to interject, I think the P&T Committee has the full monograph in front of them, which details the study a bit more on page 8. I am not sure if it specifically answers the question, but just something to throw out there.

Donna Sullivan: Katie, this is Donna Sullivan. No, we don't have it in front of me, but I can get it up real quick if we need to.

Deb Wiser: This is Deb Wiser. There was, on page 9 of that, a paragraph regarding the Decide Trial and jumping down into the statistics, patients were required to have vitamin D concentration above 12 before study entry and all subjects received 500 mg or more of calcium supplements along with daily vitamin D supplementation based on baseline vitamin D measurements. After 12 months of therapy, the denosumab significantly increased bone marrow density at the total

hip 3.5% compared with alendronate, 2.6% with a PE of 0.001, and the sample size was 594. That's about the level of statistics we've got.

Barak Gaster: Great. Thanks so much, Deb.

Kevin Leung: Okay. And if there are any questions later on, I can pull up that study, as well. All right, moving forward to slide eight, safety considerations. The average GI reaction for bisphosphonates occurs in a third of all patients. The most common adverse reaction includes GI problems, inflammation of the esophagus, and gastric ulcers, hence the recommendation for oral bisphosphonates to have patients who stand or sit upright for at least 30 minutes after taking their medication. The GI reactions are mitigated with the usage of IV therapy. Osteonecrosis of the jaw developed in cancer patients that were on doses 10 times higher than doses used for osteoporosis. The incidents of osteonecrosis of the jaw was similar to that of bisphosphonates in a large randomized control trial comparing denosumab and zoledronic acid.

Moving on to slide nine, the safety considerations for the other products. With SERMs, raloxifene, the most serious adverse effect associated with raloxifene was that of approximately a three-fold increased risk of ETE. Statistically significant higher incidents of hot flashes, arthralgia, dizziness, leg cramps, influenza-like symptoms, endometrial fluid, peripheral edema, and worsening diabetes were also found with raloxifene compared with the placebo. But on a positive note, the largest study of raloxifene found that it may have a protective effect with reducing the risk of all types of breast cancer.

Moving forward with denosumab the average effects include back pain, limb pain, musculoskeletal pain, hypercholesterolemia, and urinary bladder infections were the most common adverse effects reported with denosumab. Serious adverse events included hypocalcemia, severe skin and other infections and dermatologic conditions including dermatitis, rashes, and eczema.

Denosumab is contraindicated in patients with hypocalcemia and may worsen, particularly in patients with severe renal impairment. These patients should receive a supplement of calcium and vitamin D. Because denosumab significantly suppresses bone turnover and the

increased risk for osteonecrosis of the jaw, atypical fractures and delayed fractured healing, the FDA therefore requires risk evaluation and mitigation strategy runs including a medication guide for patients and information for healthcare providers regarding the risks and benefits of denosumab.

Finally, on slide ten, to conclude, considering bone mineral density, history of fractures, and other clinical risk factors prior to starting the patients on these pharmacologic therapies, and our next point oral alendronate, risedronate, and ibandronate appears to have comparable efficacy and safety and should be considered first-line agents for prevention and treatment of osteoporosis. However, for patients that have serious GI side effects and tolerance issues, IV bisphosphonates, such as IV ibandronate or zoledronic acid may be preferred for those specific patients, and teriparatide and denosumab should be reserved for patients who are at high risk of fractures, as defined by multiple risk factors, prior history of fractures, or with severe osteoporosis. At this point, this concludes the presentation. Are there any questions?

Christopher Smith: This is Christopher Smith. Could you clarify with more detail your reason for saying that alendronate and its equivalent oral agents are your first-line choice… your first-line recommendation? You just kind of flushed that out a little bit.

Kevin Leung: The main reason is that most of the studies that have been… there have been more studies that have been conducted for the bisphosphonates compared to the other therapies, and according to the national guidelines, there is more support on utilizing these products. Specifically, the concerns on the side effect profiles of these other medications need to be monitored more, and with the bisphosphonates, the main concern has historically been the GI upset. There has been research and studies in the past couple of years that have expressed concern on utilizing the bisphosphonates for more than five years, because of an accumulation of the ingredient in your system, and there have been discussions on setting up drug holidays for these products.

Barak Gaster: This is Barak Gaster. I also would just like to circle back to the additional data that Deb brought out for us from the monograph, which is that the difference in bone marrow density is not terribly dramatic, and that this is a difference between denosumab and alendronate for

bone marrow density only and not for difference in fracture risk, and so I think sort of speaking to what the ODS representative was just saying that I think that there is much less data on the efficacy of denosumab for actually preventing fractures, as opposed to effecting bone mineral density, which is the more clinically significant outcome.

Deb Wiser: This is Deb Wiser, and additionally from what I saw, denosumab had shorter-term studies and doesn't have any longer-term data. I think it only goes out to a year at this point.

Barak Gaster: This is Barak Gaster. So, in terms of safety, as well, I think there are more open questions. Are there other questions from the committee for ODS on the presentation? Okay, we have one speaker stakeholder who would like to give a presentation. This is Claire Merinar from Amgen. So, if you could please come up to the microphone. And I'll just remind you that you have three minutes. Thanks.

Claire Merinar: All right. Thank you very much for the opportunity to speak today in support of Prolia. I am Claire Merinar, and I'm a medical liaison with Amgen. So, Prolia is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, which is defined as a history of osteoporotic fracture, or multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapies.

In addition, Prolia actually recently received FDA approval, as a treatment to increase bone mass in men with osteoporosis at high risk for fracture. Prolia is also indicated as a treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy, for nonmetastatic prostate cancer, and as a treatment to increase bone mass in women at high risk for fracture who are receiving adjuvant aromatase inhibitor or AI therapy for breast cancer.

So, firstly, Prolia has a unique and targeted mechanism of action. It's the first and only FDA approved RANK ligand inhibitor. Prolia prevents RANK ligand from activating its receptor RANK on the surface of osteoclasts and their precursors. So, by preventing this interaction, you're actually inhibiting osteoclasts formation, function, and survival thereby decreasing bone resorption and increasing bone mass and strength both cortical and trabecular bone compartments.

Prolia can also be considered for use in patients with renal impairment and dose adjustments are not required.

Secondly, Prolia has shown robust fracture reduction in women with postmenopausal osteoporosis at vertebral and nonvertebral and hip sites. In the Pivotal Phase 3 Fracture Study in women with PMO, Prolia significantly reduced the incidents of new vertebral fracture by 68%, nonvertebral fracture by 20%, and hip fractures by 40% versus placebo at three years, and Prolia has also significantly increased BMD at all anatomic sites measured at three years.

In addition, Prolia has been studied up to six years in the open label extension study of the Pivotal Phase 3 Fracture Study, and we continue to see BMD increases through those six years.

Prolia is also the first and only FDA approved treatment for cancer treatment induced bone loss or CTIBL. In the Pivotal Phase 3 Study in men with nonmetastatic prostate cancer receiving ADT or androgen deprivation therapy, Prolia significantly reduced the incidents of new vertebral fractures by 62% versus placebo at 36 months.

Prolia also significant increased lumbar spine BMD versus placebo at 24 months and in addition, there is a Pivotal Phase 3 Study of women with breast cancer receiving aromatase inhibitor therapy, and in that particular study Prolia significantly increased lumbar spine BMD versus placebo at 12 months. For fair balance, I also want to touch on safety information. In the Pivotal PMO Fracture Study, there were no significant differences between patients who received Prolia and those who received placebo in terms of total incidence of adverse events and serious adverse events or discontinuation of treatment due to adverse events, but per the prescribing information, Prolia is contraindicated in patients with hypocalcemia, serious infections including skin infections may occur, including those leading to hospitalization, dermatitis, rashes and eczema, as well as osteonecrosis of the jaw and atypical femoral fractures have also been reported. Again, I would refer you for additional detail to take a look at the Prolia prescribing information.

Lastly, Prolia is administered subcutaneously once every six months, which does offer a convenient dosing option for both patients and their physicians. While clinical trials have demonstrated the efficacy of available pharmacologic treatments at reducing fracture risk, real world utilization data suggests that patients may have difficulty adhering to these therapies. Low compliance may be associated with increased incidental fracture.

So, in summary, I would respectfully ask the committee to consider maintaining Prolia on the formulary, because of the following attributes. It has a unique and targeted mechanism of action, efficacy in both postmenopausal osteoporosis, male osteoporosis, and cancer treatment induced bone loss. In addition, Prolia is the first and only agent approved for cancer treatment-induced bone loss. Then lastly, Prolia is administered once every six months, which does offer a convenient dosing option. At this time, I yield any additional time to the chair unless there are questions, and I thank you again for your consideration.

Barak Gaster: Thank you. All right. So, we have the ODS still on the line, and I think that we may want to release you guys until after lunch and then after lunch we'll do the next one.

Donna Sullivan: Correct.

Barak Gaster: Okay, great. So, thank you very much ODS for the presentation, and we will reconvene with you again at 1:30 to talk about the erythropoietin stimulating agents.

Kristin Sisourath: Thank you very much.

Kevin Leung: Thank you.

Barak Gaster: All right. So, this is Barak Gaster. We now turn our attention to a motion on the bone density regulator drug class. This is Barak Gaster. I sort of turn the committee's attention to the drug utilization report that we have in addition to the material in our binder.

Susan Rowe: This is Susan Rowe. I have a question about this, Donna, if you know. On the alendronate particularly, do you know how the usage breaks down in daily versus weekly dosing?

Donna Sullivan: I didn't put it on here, but I might be able to find that out, if you give me a few minutes. I could dig it up.

Susan Rowe: Thank you.

Donna Sullivan: Did you want me to go through the rest of the information first on the cost analyses or do you want me to?

Susan Rowe: No, absolutely.

Donna Sullivan: Okay. It'll probably take me a few minutes.

Barak Gaster: Okay. This is Barak Gaster. I think that's a great question. I mean, there used to be a big difference between the daily administration and the weekly administration in terms of cost, but that may no longer be the case. So, it would be useful for us to know.

This is Barak Gaster. I have a quick question for Chuck. Oh, never mind. Never mind.

Donna Sullivan: And so, Dr. Rowe, was your question specific to alendronate or all of the bisphosphonates that have multiple dose daily versus weekly?

Susan Rowe: You know, Donna, this is Susan Rowe. I think we could take either information, but I was specifically interested in alendronate, since it is the majority of our clients that would receive a product out of this class.

Donna Sullivan: Okay. So, I have the actual claim data. So, I'm not able to show it to you on this screen, and just looking… I mean, I'm just scrolling through here, and it looks like the majority of the claims are for the 70 mg and the 35, and there's just a couple in the 10 mg range and the 5 mg range.

Susan Rowe: Okay.

Donna Sullivan: So, it looks like people are taking the longer-acting product.

Susan Rowe: Okay, good. Thank you.

Barak Gaster: And this is Barak Gaster. So, that's reassuring that the very low average cost per use or per month that we're seeing is for the weekly administration?

Donna Sullivan: Yes, and so what is represented here in the cost analyses in front of you is I had our analyst roll them up to you know kind of like the brand name level. So, it's all alendronate products whether they're immediate release or extended release are reflective in the price here, as are all of the other products, as well, so.

Barak Gaster: Great.

Christopher Smith: This is Christopher Smith. I would like to just start the discussion by looking at this utilization reflecting that this is already quite an attractive spread in regards to what patients are currently receiving, and recognizing that there are often clinical indications for alternatives to alendronate for a minority of patients that is reflected here, as well. I am questioning what gains can be made in regards to placing formulary restrictions in this drug class?

Barak Gaster: This is Barak Gaster, and I agree that it does not look like there is a tremendous amount of improvement in terms of utilization and that is probably the reason that this class has not come up for us before and that… but I would suggest that one of the advantages would be if some of the newer agents, which are not necessarily better or safer and are much more expensive would have an increasing utilization moving forward in terms of… that this is data that is current as of when, Donna?

Donna Sullivan: This was data that was pulled for the fiscal year… or I'm sorry, calendar year 2011. We excluded the managed care population, or the people that were going to be moving to managed care. We excluded their claims. Then, we pulled medical and pharmacy claims. So, where you see under diagnoses where it says pharmacy claim, that was filled at a retail pharmacy, so we don't have the specific diagnoses, but the medications where it says osteoporosis or bone metastases. Those

were the medical claims and so we were able to get the diagnoses associated with that claim when we pulled the data.

Barak Gaster: This is Barak Gaster. What was the date of FDA approval for Prolia?

Donna Sullivan: It was just recently. I'm not exactly sure what the specific date was.

Barak Gaster: Could the representative from Amgen?

Claire Merinar: It was initially approved in June or July of 2010.

Donna Sullivan: So, June or July of 2010.

Barak Gaster: Great. Thank you.

Chuck Agte: This is Chuck Agte. Was that the approval date or your market date, as well?

Claire Merinar: Approval and marketing.

Barak Gaster: This is Barak Gaster. I'm just sort of raising the possibility that use of Prolia may be more in 2012, although it's difficult for us to say that without having that data, but in sort of the global question that Dr. Smith raised as to the advantage to setting a formulary for this drug class, I think that there are potential cost savings that could be accrued.

Susan Rowe: This is Susan Rowe. So, in looking at this, everything that's not a pharmacy claim, mysteriously is also an injection. So, we're getting that because it's being administered, probably in an infusion center. The things like the Prolia, maybe the Boniva injection, the Reclast would usually be given in an outpatient hospitalized or office type setting. It's not usually something that the patient would give. What currently do our clients need to… is this a preauthorization? How do our clients currently get this?

Donna Sullivan: So, right now, if they get it, I believe, and Chuck and Amy can correct me if I'm wrong, that there's no restrictions on these medications through the medical benefit. However, we intend to implement the formulary across the medical benefit. So, if there was a nonformulary product, then the physicians would have to go through the same

nonformulary justification process in order to administer a nonformulary drug, even within the physician's office. So, it's our intent to have the same criteria across the board for all of the medications, and that's why we included the injectables within this class.

Chuck Agte: This is Chuck Agte. Unfortunately, when we pulled the data for it, we do have a sheet out there for the coverage and restrictions. The coverage status that appears on that, at this point in time, is specific to the pharmacy coverage status. Some of the drugs on the list in front of you that are professionally administered do require PA and others don't and off the top of my head I don't know all of them, but I believe, and I could double check, Prolia does in fact require prior authorization at this time, which would be requested by the physician's office, and I am not sure of the others, but I think Boniva may require prior authorization, as well, but I can find out hopefully in the next few minutes here.

Susan Rowe: This is Susan Rowe. My experience in working with our patients is that, and I can't speak for DSHS, but if we refer someone for a Reclast injection, that's prior authorization no matter who their insurance, you know? So, the more standard insurances put that through.

Chuck Agte: Yes, I believe Reclast is also on PA. I am working from memory at the moment, so let me actually verify what does or doesn't require PA on the medical benefit side.

Christine Klingel: This is Christine Klingel. We have it in our packet if this is correct. After the presentation, there's the current Medicaid status and restrictions, and they do have Reclast and Prolia listed as prior authorization, if that's correct?

Chuck Agte: Those are, as I said, this particular status and restrictions table is for pharmacy claims.

Christine Klingel: Okay.

Chuck Agte: So, let me, again, verify what we're actually doing on the professionally administered side.

Deb Wiser: This is Deb Wiser. Just observing amongst the oral bisphosphonates, there does appear to be a significant cost difference between the alendronate and the other oral bisphosphonates with equivalent efficacy and side effect profile. It seems like we could narrow it down some there.

Christopher Smith: This is Christopher Smith. To follow up on that comment, can members of the committee speak from their clinical experience regarding the advantage of oral Boniva over oral alendronate and why prescribers might choose that? I understand it's an agent that's taken less often. So, compliance and convenience are factors. Can people address that? The reasons why some prescribers might choose that?

Mason Bowman: This is Mason Bowman. As far as I know, not from a prescribing side but just from the pharmacy side, that really is the reason for adherence, the once-monthly dosing, but as far as significance in efficacy between the two, I really am not convinced that there is much of a difference.

Susan Rowe: This is Susan Rowe. This is a class of drugs, though, that has a very, very low patient adherence. So, as much as we can increase that would be advantageous.

Eric Harvey: This is Eric Harvey. I'm not familiar with any evidence that shows that once-monthly dosing actually increases adherence over once-weekly dosing. So, I would love to see that information and make a decision based on it.

Barak Gaster: This is Barak Gaster. I think the two questions that we have are what indications we would put in our motion and then what medications we would include or exclude on the formulary and we probably want to keep the list of indications simple and so we could, in a simplest way, just make the indication be osteoporosis.

Eric Harvey: I would agree with that. I would also point out that pamidronate has some specific indications for use in oncology around bone metastases and hypercalcemia malignancy, and we may need to call that out as part of this.

Donna Sullivan: This is Donna Sullivan. So, with the monograph, I had… for the indications that were in the monograph, it really focused more on

osteoporosis, so I specifically left those products off of the indication table that is in your packet, and we also left off the products that were only… I think there's a denosumab and a zoledronic acid product that are… specifically have cancer-related diagnoses, and so we did not include those in the class either. So, I just wanted to point that out to you. So, we have… in your packet, there is a table of the indications for men or women for all of the drugs within the class. So, maybe stick to those indications in your motions, and if you're silent on the hypercalcemia and malignancy, then those drugs would remain formulary for those indications that you do not address today.

Christopher Smith: This is Christopher Smith. In addition to osteoporosis, I believe we have to include patients with a history of fragility fracture or some other terminology for those that don't specifically meet the criteria of osteoporosis but still have a history of a significant fracture related to fragile bones.

Donna Sullivan: Correct.

Susan Rowe: This is Susan Rowe. I also, just… the majority of agents that we're talking about here are bisphosphonates, but I do think therapeutically there is a place for a variety of mechanisms for physicians to try and treat osteoporosis. So, some consideration by our board of calcitonin, raloxifene, and where is their place, and I'm not saying that they have to be there, but I would like that discussion.

Barak Gaster: This is Barak Gaster. I definitely appreciate that, and I think that we still may want to limit the formulary to bisphosphonates and have those other agents that can have a place in therapy have prior authorizations that would try to identify the unique situations in which a clinician may want to prescribe one of those agents instead of a bisphosphonate.

This is Barak Gaster. So, Chuck, right now, or Donna and/or Chuck, so I'm noticing that like, so for instance, if you look at the drugs that currently are covered versus require prior authorization that raloxifene does not require any prior authorization and neither does calcitonin, and I am wondering if there has been sort of clinical consideration as to introducing prior authorization for those agents?

Donna Sullivan: This is Donna. I will defer that to Nicole and see. Can you explain why those are not on prior authorization?

Nicole Nguyen: So, that was… I think at one time Evista might have been [inaudible] authorization and was removed, but it hasn't… they just haven't been reviewed or considered. I think we've talked in the past about bringing in the bisphosphonates as part of the PDL, but it never was felt to be beneficial to go through the PDL process with these. So, they just never were, with Medicare Part D, come in and taken a lot of those clients and I think it just never was reviewed for those reasons.

Barak Gaster: So, this is Barak Gaster. I guess I would come back to, you know, for our purposes of setting a tier 1, this is the drug that's on the formulary and all the others are certainly available to clinicians with justification makes sense and that by excluding raloxifene and calcitonin from our formulary, we are in no way barring clinicians from using those agents in clinically appropriate situations.

Christopher Smith: This is Christopher Smith. Is it our responsibility to define those situations? Remind me again, Chuck, how the prior authorization process works?

Chuck Agte: Okay, so can you… seeing as how I just walked back in from checking with my staff, can you reiterate what the question was?

Christopher Smith: Well, we are looking limiting the formulary to alendronate specifically and wondering, as the chair has proposed, certainly the other drugs could be available given the right circumstances, and I'm wondering whether it's up to the committee to define those circumstances or whether those are already clinical issues that you had established?

Chuck Agte: So, depending on the diagnosis that you address, if you do not address a diagnosis… and it also depends… so, I guess, let me ask the clarifying question. Are you talking about leaving product out of your formulary decision or excluding them from the formulary?

Christopher Smith: The latter.

Chuck Agte: Okay. So, if you exclude a product from the formulary for a particular diagnosis, it is still potentially available to Medicaid patients through

the nonformulary justification process, which would involve the physician essentially letting us know why whatever product you have left on the formulary would not be appropriate for the patient, either because they have in fact failed them, had adverse reaction, why it's inappropriate for them to take it at all. So, as… that's the condition for anything, which is nonformulary is why is what is formulary not appropriate for the patient to take.

Christopher Smith: Christopher Smith. But then your response to that request is based upon what factors? Whether it's a convincing argument? Whether it meets certain clinical criteria that have been preestablished? The budget that month? How would you determine that?

Chuck Agte: That would be reviewed by our clinical reviewers, primarily Nicole Nguyen sitting here, and we have a couple of physicians who also review some of the physician-based claims, and so it would be a matter of… it's relatively straightforward in why can't the client take the formulary product? So, yes there is some element of a convincing argument, but it's a fairly low threshold if you've documented, you know, client was on the formulary product for X months with no improvement. Client was on formulary product and had intolerable side effects. Client can't take formulary product because they have a disease state, which contraindicates its use. So, it's fairly straightforward criteria.

Barak Gaster: This is Barak Gaster. So, I think that we would… that I, at least, would feel comfortable having those… having specifically calcitonin and raloxifene excluded from the formulary with the understanding that with a nonformulary justification those agents would be very available to the fee-for-service Medicaid population.

So, this is Barak Gaster. I think I'm coming back to the first of the two questions that I spoke about us needing to address. So, the first being the list of indications that we are going to include in our motion and as I stated, the simple indication of osteoporosis is the simplest motion for us to make. Dr. Smith raised the question of history of recurrent fractures. I think that we can, by just stating an indication of osteoporosis, that can include glucocorticoid-induced osteoporosis without us specifically stating the subtype of osteoporosis. Any thoughts from the committee on the question of calling out the

question of treatment of osteoporosis versus prevention of osteoporosis in our motion?

Mason Bowman: This is Mason Bowman. I'm not sure if I'm going to be able to address that question specifically, Dr. Gaster, but I was thinking what if we were to just state that we'll cover for all accepted approved… FDA approved conditions for osteoporosis, which would then include all the treatment and prevention of? Does that make sense, or did I confuse everybody?

Christopher Smith: Christopher Smith. I believe we need to be explicit in our wording, Chuck?

Chuck Agte: The more explicit, the better, yes.

Christopher Smith: And so, it's… the prevention category is for those patients who are on high-risk medications typically, and that is often seen in a rheumatology setting, for instance. So, that group also would need to be included.

Barak Gaster: This is Barak Gaster. So, if we limit our motion to the indication of osteoporosis alone, how does that impact somebody having covered one of these bone-regulating medications for the prevention of osteoporosis?

Chuck Agte: If you don't specifically address prevention, then all products with an FDA indication for prevention would remain formulary for that indication.

Barak Gaster: So, this is Barak Gaster. Are we currently looking for a confirmation of a diagnosis at the time of paying a claim for any of these medications?

Chuck Agte: For the ones which are physician administered or professionally administered, I am still waiting on confirmation from my staff. I believe all of them require prior authorization at this time and I do not… I would actually rely on Nicole, although she does not review the physician claims, to have a better knowledge of what we actually look for in diagnosis and whether we look at prevention.

Donna Sullivan: And this is Donna Sullivan. I think I can actually address Barak's question. So, if you were to say for the treatment of osteoporosis and were silent on prevention, then the drugs that are indicated for preventing osteoporosis would remain formulary for that particular indication. So, if we had Reclast, and if you said, it's not formulary for treatment of osteoporosis and the claim comes, or a prior authorization request comes in for the prevention of the osteoporosis for patients that are at risk factors, then it would be allowed. So, there would be some sort of criteria or an EA code, if it was on the POS side for drugs that have the indications, FDA labeled indications, that you do not specifically address.

Barak Gaster: Okay. This is Barak Gaster. So, I think that we do want to have perhaps as our two indications the prevention and treatment of osteoporosis, and this is… the question is sort of what about somebody who has had recurrent fractures without osteoporosis? It gets to sort of what exactly is the clinical definition of osteoporosis?

Donna Sullivan: This is Donna Sullivan. So, if you look at the indication table that's in your packet, there is… almost all of the drugs are indicated for the treatment of osteoporosis. Nearly all of them are. Most of them also have an indication for the prevention, and then there are two that are indicated for the treatment of postmenopausal women with high-risk of fracture and treatment of other women at high risk of fracture. So, if you don't specifically say those, then those will remain formulary. All of those products with those indications remain formulary for those specific indications.

Barak Gaster: This is Barak Gaster. I now direct the committee's attention to slide number three of the monograph. In terms of the evaluation of osteoporosis and this is what I was remembering, which is that the specific definition of osteoporosis is that the diagnosis can be made from a bone mineral density score or a history of fragility fracture. So, I think that calling these out at separate indications is not necessarily clinically needed, given that the diagnosis of osteoporosis can be made on the basis of bone mineral density score or history of fragility fracture.

Christopher Smith: This is Christopher Smith. I would agree.

Christine Klingel: This is Christine Klingel. One other thing that we could add based on the T-scores is osteopenia, because that would include the prevention then. Patients are often put on a lower dose when they are diagnosed with osteopenia.

Deb Wiser: This is Deb Wiser. It's indicated in the setting of osteopenia in addition to having a higher risk profile, as generally calculated by the FRAX score. So, it would be the combination of osteopenia and other risk factors.

Barak Gaster: This is Barak Gaster. I would suggest that rather than wading into the question of osteopenia that we leave our indications relatively broad being the prevention or treatment of osteoporosis.

Deb Wiser: This is Deb Wiser. I agree.

Barak Gaster: So, then we turn our attention to the second question, which is, which drugs from this class to include or exclude for these two indications, and I would suggest that we could keep it very simple and have alendronate be included and have the other drugs, other than alendronate, be excluded but clearly still be available with formulary, what's the term? Formulary?

Chuck Agte: Nonformulary justification.

Donna Sullivan: This is Donna Sullivan. So, Dr. Gaster, did you specifically name any drugs that you want excluded, or the ones that you wanted to remain?

Barak Gaster: So, what I suggested was that alendronate be included and all other drugs other than alendronate be excluded.

Chuck Agte: Would that specifically be generic alendronate?

Barak Gaster: It would be specifically generic alendronate.

Christine Klingel: This is Christine Klingel. So, I noticed… so, again remind me. I know you've told us a hundred times. So, if a patient then say is using… because we have estrogen listed up there, and they are using estrogen for something other than the prevention of osteoporosis, obviously say for hot flashes, they're not going to get a reject at the

pharmacy level, correct? Or would they get a reject and have to have some sort of justification that they're not using it for osteoporosis, they are using it for hot flashes?

Donna Sullivan: This is Donna Sullivan. Estrogen was mistakenly added to this slide, and it should not be considered part of the bone density regulators. Estrogen products are governed by our preferred drug list process, and so that will not change.

Christine Klingel: Okay. Good. Thank you.

Chuck Agte: And that's actually also an important consideration for the board is that estrogens, when used for prevention of osteoporosis or treatment of osteoporosis, because they are part of the PDL, remain a formulary option for patients without other authorization other than PDL criteria.

Christopher Smith: This is Christopher Smith. In the wording, Donna, I think in the third line, medically accepted indication… indications of the treatment and prevention.

Donna Sullivan: This is Donna Sullivan. We used the term, or phrase, medically accepted conditions, I believe, because that is the terminology in the Federal Statute that medically accepted condition is FDA labeling and/or supported in the compendia. So, and I can leave it as indication, but it…

Christopher Smith: This is Christopher Smith. I'm just trying to think about how you phrase that. Is the treatment of osteoporosis a condition?

Chuck Agte: This is Chuck Agte. The actual federal wording is medically accepted indication, and medically accepted indication by definition covers any FDA labeled use of a product and any use of a product that is supported in the compendia, which are Drugdex and AHFS.

Christopher Smith: Thank you.

Donna Sullivan: I understand what you're saying now, Dr. Smith.

Chuck Agte: And just for the record, this is Chuck Agte, because I have my insert back, in regard to the physician administered products, professionally

administered drugs currently, the Boniva and Aredia do not require authorization, and the, let's see, Reclast and Prolia both require authorization. It's not clear from the message, but some of those products, which are otherwise covered without PA, do have diagnosis restrictions, which, since they sent me diagnosis code, which I don't know off hand, 731 and 733, which I am presuming are osteoporosis, but we'd have to further look those up.

Donna Sullivan: So, Dr. Smith, I have changed the language to say after reviewing the clinical information for the drugs within the bone density class with the medically accepted indications, prevention, and treatment of osteoporosis, does that make more sense than we had it before?

Barak Gaster: This is Barak Gaster. I think we want to be calling this the bone density modulating class.

Christopher Smith: Just stick the word “the” in front of prevention.

Michael Johnson: This is Michael Johnson. Does this include the secondary glucocorticoid induced, or do we have to add that in there somewhere? Or is this enough?

Chuck Agte: Speaking generally to osteoporosis, if you're not more specific, that would encompass all subsets of osteoporosis.

Barak Gaster: All right. This is Barak Gaster. Any other questions, comments, suggestions for our motion? Is there anybody who would like to make this motion?

Deb Wiser: This is Deb Wiser.

Michael Johnson: This is Michael Johnson. After reviewing the clinical information for the drugs within the bone density modulating class with the medically accepted indications, the prevention and treatment of osteoporosis, I move that no single brand or generic drug product in this class has a significant clinically meaningful therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment and prevention of osteoporosis for any subpopulation. The branded products within this class do not have a significant meaningful clinical advantage over their generic equivalents and are excluded from the formulary. In light

of their clinical equivalence and after review of the average cost and drug utilization data of the medications in this class, all drugs, except generic alendronate, shall be removed from the formulary in favor of less costly alternatives.

Barak Gaster: This is Barak Gaster. I second that motion. All in favor say, aye.

Group: Aye.

Barak Gaster: All opposed, same sign. So, that motion passes.

Donna Sullivan: So, Dr. Gaster, this is Donna Sullivan. So, we have 20 minutes before the scheduled lunch break. Would you like to shift back to the agenda previously and cover the dyslipidemia drugs before lunch or get as far as we can prior to the lunch break?

Barak Gaster: Yes. This is Barak Gaster. I think we should.

Donna Sullivan: Okay. Thank you.

Barak Gaster: All right. This is Barak Gaster turning the committee's attention to the motions, which we have previously passed in this drug class and reminding us of the considerable deliberation that we went through to arrive at the three motions, four motions—four motions for various subclasses within this drug class. I think that we want to stick with the whys deliberating that we did at our June meeting and we want to try to revise these, as simply as possible, to include the better justification for the decisions that we made. So, it should be a relatively straightforward process of including the language about generics and including the language of review and consideration of cost considerations.

Donna Sullivan: Pretty soon, we'll be using the bone density regulators to treat hypercholesterolemia. Okay. This is Donna Sullivan. I think I have it put into the new format.

Chuck Agte: Donna, for this, this is Chuck Agte. For this particular drug class, I believe the original motion and indications we are addressing, there appear to be three of them, and I think you captured two, unless I'm misinterpreting there.

Donna Sullivan: Well, there's four different motions.

Chuck Agte: For this drug class specifically, we had listed mixed dyslipidemia, primary hyperlipidemia, and hypertriglyceridemia.

Donna Sullivan: I see that, sorry.

Barak Gaster: This is Barak Gaster. That looks very good. Would anyone like to make this motion?

Christine Klingel: This is Christine Klingel. I'll attempt it. After reviewing the clinical information for the drugs within the dyslipidemia fibric acid derivative and bile acid sequestrant drug classes for the treatment of medically accepted indications of mixed dyslipidemia, primary hyperlipidemia and hypertriglyceridemia, I move that no single brand or generic drug product in this class has a significant clinically-meaningful therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment of mixed dyslipidemia, primary hyperlipidemia, and hypertriglyceridemia for any subpopulation. The brand of products within the class do not have a significant meaningful clinical advantage over the generic equivalents and are excluded from the formulary. In light of their clinical equivalence and after review of the average cost and drug utilization data of the medications in this class, all branded drugs shall be removed from the formulary in favor of less costly alternatives.

Deb Wiser: This is Deb Wiser. I second.

Barak Gaster: All in favor say, aye.

Group: Aye.

Barak Gaster: All opposed, same sign, and that motion passes.

Christopher Smith: One just grammatical thing. After the word accepted indications in the first sentence there in the fourth line, you can remove that comma. Thank you.

Barak Gaster: And now, this is Barak Gaster. We turn our attention to the Lovaza motion, in which the drug subclass is swapped in.

Susan Rowe: This is Susan Rowe. I wonder on these last three motions, they're not broad sweeping motions. They were specifically written to take drugs off the formulary, and we took them off, because of the clinical considerations, which these motions do say. Do we need to add anything to that?

Barak Gaster: This is Barak Gaster. I would agree that for these last three motions and these specific agents that we excluded, we were excluding them primarily because of a lack of efficacy data, and even if they were cheap, I'm not sure that we would want to cover them. So, I would agree that unless you feel strongly otherwise, in terms of defensible regulatory position that these last three motions could stand perfectly soundly on clinical grounds alone.

Chuck Agte: I'm still thinking. Give me just a sec.

Christine Klingel: This is Christine Klingel. With the exception probably of the second one, those combo classes do contain medications that we have found or we have included elsewhere in the formulary. It was just those particular combo products that we excluded.

Susan Rowe: This is Susan Rowe. Are those other products still covered by the PDL?

Chuck Agte: Right. Those were specifically addressed because combination products are excluded from the PDL.

Donna Sullivan: This is Donna Sullivan. I think we still need… so, if you said that there's a clinical reason why you removed the products from the PDL that you need to say that you feel that they are less effective or there's lack of evidence showing that they're more effective or as effective.

Barak Gaster: This is Barak Gaster. I mean, certainly part of our rationale for removing them was their very high cost. So, I don't think it's wrong for us to include that as part of our justification.

Chuck Agte: Yes, and that's what I was just, this is Chuck again, that I was looking at is that beyond the fact… we do still need a reason, whatever it might be, beyond the fact that they qualified for exclusions. So, whether it was cost or whether you felt there was lack of clinical efficacy, whatever the reason is, we need to know the reason beyond we could exclude them so we did. We need to know the why you did.

Barak Gaster: Great. This is Barak Gaster. This motion now looks very good, and so I will read it. After reviewing the clinical information for the drugs within the dyslipidemia anti-hyperlipidemics drug class for the treatment of the medically accepted indications of mixed dyslipidemia and hypertriglyceridemia, I move that no single brand or generic drug product in this class has a significant clinically-meaningful therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment of mixed dyslipidemia and hypertriglyceridemia for any subpopulation. The brand of products within the class do not have a significant meaningful clinical advantage over their generic equivalents and are excluded from the formulary. In light of their clinical equivalence and after review of the average cost and drug utilization data of the medications in this class, Lovaza shall be removed from the formulary in favor of less costly alternatives.

Deb Wiser: This is Deb Wiser. I second.

Barak Gaster: All in favor say, aye.

Group: Aye.

Barak Gaster: All opposed, same sign. So that motion passes, as well.

This is Barak Gaster. Thank you, so much, Donna. Very well done. I will read this one. After reviewing the clinical information for the drugs within the dyslipidemia HMG-CoA reductase classes for the treatment of medically accepted indications of mixed dyslipidemia, primary hyperlipidemia and other labeled indications, I move that no single brand or generic drug product in this class has a significant clinically-meaningful therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment of mixed dyslipidemia, primary hyperlipidemia, and other labeled indications for any subpopulation. The brand of products within the class do not have a

significant meaningful clinical advantage over their generic equivalents and are excluded from the formulary. In light of their clinical equivalence and after review of the average cost and drug utilization data of the medications in this class, Avacor, Caduet, and Simcor shall be removed from the formulary in favor of less costly alternatives.

Christine Klingel: This is Christine Klingel. We just missed combination, HMG-CoA reductase class combinations and then I'll second.

Mason Bowman: This is Mason Bowman. It needs to say HMG-CoA reductase inhibitor combination drug.

Barak Gaster: Great. So, all in favor of this revised wording say, aye.

Group: Aye.

Barak Gaster: All opposed, same sign. So, that motion passes. There is one final motion.

This is Barak Gaster. So, at the top on the fourth line I think rather than drug classes, it could just be drug class.

This is Barak Gaster. Any other thoughts, corrections? Great. So, I will go ahead and read it. After reviewing the clinical information for the drugs within the dyslipidemia intestinal cholesterol absorption inhibitors and their combinations drug class for the treatment of medically accepted indications of mixed dyslipidemia, primary hyperlipidemia and familial hypercholesterolemia, I move that no single brand or generic drug product in this class has a significant clinically-meaningful therapeutic advantage in terms of safety, efficacy, or clinical outcome for the treatment of mixed dyslipidemia, primary hyperlipidemia, and familial hypercholesterolemia. The brand of products within the class do not have a significant meaningful clinical advantage over their generic equivalents and are excluded from the formulary. In light of their clinical equivalence and after review of the average cost and drug utilization data of the medications in this class, Vytorin and Zetia shall be removed from the formulary in favor of less costly alternatives.

Susan Rowe: This is Susan Rowe. I will second the motion.

Barak Gaster: All in favor say, aye.

Group: Aye.

Barak Gaster: All opposed, same sign. And that motion passes, which completes our review/revision of the motions on the antihyperlipidemic drug class. So, we convene for lunch break and will return at 1:30 to review the erythropoietin stimulating agents. Thank you.

Duane Thurman: One announcement. This is Duane Thurman. I just want to remind the committee that we're going to close the room for lunch to leave you guys alone, but for the open public meetings and reasons please refrain from discussing any official committee business during that time.

Barak Gaster: All right. Good afternoon, everybody. We are going to reconvene, as the Drug Utilization Review Board, and the next topic that we are going to cover is the erythropoiesis-stimulating agents, and we have a presentation to hear. I think the speaker is on the line. Are you on the line?

Vafa Mahboubi: I'm here, yes.

Barak Gaster: Great. So, why don't you go ahead and take it away. Thank you, very much.

Vafa Mahboubi: Okay. Thank you. Once again, my name is Vafa Mahboubi. I am a pharmacist here, and I will be reviewing the erythropoiesis-stimulating agents, and I understand that you guys have a copy of the slides, correct?

Barak Gaster: That is correct. If you can just give us a…

Vafa Mahboubi: I'll give you a next slide… I'll give you a next slide.

Barak Gaster: Thank you.

Vafa Mahboubi: Does that sound good?

Barak Gaster: That's perfect, thanks.

Vafa Mahboubi: Okay. Sounds good. So, moving on to the next slide, recent approvals. There was a recent approval in ESA that was approved in March with Omontys, and this is only indicated in the treatment of anemia due to CKD in dialysis patients only. The real advantage to this, or one of them, is that it's administered once monthly, and it has a REMS program, but obviously, since it's only indicated in CKD and not in cancer chemotherapy, the REMS program is only part of [inaudible] healthcare professional letter. Just a brief background and introduction.

We all know how ESAs work. They work by stimulating the production of new red blood cells, the differentiation and proliferation of erythroid precursors, the synthesis of hemoglobin and the release of reticulocytes into the circulation. There are multiple treatment guidelines, since it does span multiple disease states that do review ESAs periodically, and they all consider them therapeutically equivalent.

As you can see, two of the commercially available products, Epogen and Procrit, are actually the identical chemical entity with darbepoetin and Aranesp being another commercially available product, and now obviously Omontys, as well.

The box warning also applies to all of these agents, and this really is the primary point of concern these days with using ESAs. They are all seen, as I said previously as being therapeutically equivalent. But when it comes to the safety of these products, that's where a lot of the discussion has been, and the box warning includes increased mortality or MI stroke and thromboembolism, and increased mortality and/or increased risk of tumor progression or recurrence in patients with cancer receiving ESAs.

As you can see, Epogen, Procrit, and Aranesp are all indicated for anemia of CKD and also anemia due to cancer chemotherapy with Omontys only indicated in dialysis patients, and Epogen and Procrit also having an indication in anemia due to zidovudine therapy and also a noncardiovascular surgery. One of the more common uses that is off

label for Epogen and Procrit is anemia due to hepatitis C virus treatment, and that is due to the ribavirin portion of the treatment regimen.

There are numerous comparative efficacy trial that have compared epoetin and darbepoetin, particularly in CKD and anemia due to cancer treatment, and what they've found really is that the majority of this evidence indicates that these agents are comparable. In chemotherapy, the 2007 NCCN practice guideline concluded that darbepoetin and epoetin were comparable, and this was regardless of tumor type and the degree of anemia. HRQ also found that when they did a comparative evaluation of the epoetin and darbepoetin it concluded that there is no clinical difference between the agents when it comes to safety and efficacy, as well, and a comparative review of epoetin and darbepoetin concluded that both agents have identical indications for treatment of anemia secondary to chemotherapy and have found that efficacy for both of these agents when it comes to increasing hemoglobin, decreasing the need for transfusions, and whether used at labeled dosing or extended dosing schedules, have been equal or equally as effective.

When comparing darbepoetin with epoetin, there were three randomized open label studies comparing the two in patients with nonmyloid malignancies and two studies found the regiments provided similar hematopoietic and hemoglobin response rates and decrease in transfusion requirements, and they were equally well tolerated. One study actually found that the epoetin provided an earlier response and required a lower transfusion volume, but really the application of different dose titration strategies could have played into this. So, this could have contributed to the different findings or results.

Also, a polled analysis of three similarly designed studies comparing these agents in the same dosing regimen found that these agents were clinically identical or equivalent. More of the discussion with these agents moving forward within the last few years has been appropriate use in targeting appropriate hemoglobin levels that really maximize efficacy and safety. The American Cancer Society has recommendations to initiate therapy at hemoglobin less than 10 and to maintain that between 10 and 12, whereas the NCCN differs slightly to

initiate therapy when hemoglobins are less than or equal to 11, or there is a greater than 2 gm/dL drop below the baseline.

Standard recommendations regarding discontinuing therapy apply. If the patient does not respond within six to eight weeks, epoetin therapy or ESA therapy should be discontinued, and obviously iron status for these patients should all be done periodically and at baseline.

ESA should not be used in patients not receiving myelosuppressive chemotherapy or in patients being treated with curative intent, and there is a boxed warning with regard to cancer chemotherapy specifically stating the ESA shortened overall survival and/or increase the risk of tumor progression or recurrence in cancer patients, and this was based on eight studies involving cancer patients with multiple different cancer types.

When looking at comparative efficacy and the indication of CKD, there were three randomized control studies that evaluated the efficacy and safety of CKD patients on stable doses of EPO to darbepoetin at extended dosing interval.

So, two of these studies were in adult dialysis patients and one was a pediatric study in nondialysis and dialysis patients. The conversion from EPO to darbepoetin was well tolerated and effective and children with anemia of CKD were able to maintain adequate hemoglobin levels with an extended darbepoetin dosing interval.

The efficacy and tolerability of darbepoetin once weekly was compared to epoetin twice weekly for treatment of anemia, and this was predialysis CKD patients, and both treatments provided similar hemoglobin response in a similar proportion of patients from each treatment group required transfusion and dosage adjustments.

Once again, more of the conversation, moving forward, has been optimal hemoglobin levels. One of the initiatives called Kidney Disease Improving Global Outcomes, they put out a position statement recommending hemoglobin levels should be between 9.5 and 11.5 with an increased risk at hemoglobin levels greater than 13.

And KDIGO, their last recommendations were from 2007 targeting hemoglobin levels of 11 to 12, but I think what really is now in the label for all of the ESA agents stems from the FDA MedWatch safety warning in June of 2011 that cited three key trials that showed an increased risk of death, cardiovascular events, and stroke when hemoglobin target levels were greater than 11, and it specifically states that no hemoglobin target level, ESA dose, or dosing strategy does not increase these risks. So, what was recommended that treatment should be initiated when hemoglobin levels are less than 10 in nondialysis patients. The dose should be reduced if hemoglobin levels are greater than or equal to 10, and in dialysis patients, it's hemoglobin levels greater than or equal to 11. I'm sorry, I'm not queuing you, am I? I apologize.

Donna Sullivan: What slide are you on?

Vafa Mahboubi: I'm kind of moving right along. I think I'm just used to having the WebEx available. My apologies. So, now we're on slide 13. One of the more common off-label uses with ESAs is its use in hepatitis C and the AASLD actually in their most recent guidelines for the treatment of genotype 1 chronic hep C virus infection, they do have recommendations now when it comes to anemia due to treatment of hepatitis C virus, specifically in both boceprevir and telaprevir clinic trials. This is Victrelis and Incivek, and they recommend that a dose reduction of ribavirin really should be the initial response to management of anemia, because they found that a dose reduction really had no effect on sustained virologic response rates, and actually in the telaprevir Incivek trials, the use of ESAs was not permitted.

Since boceprevir therapy is longer in duration than telaprevir therapy, anemia is most likely to be greater in boceprevir containing regimens, but really you do have to weigh the risk versus benefit when using ESAs in this population considering it is off-label use. There is documented risk of adverse events or effects with the use of ESAs, and they are costly, so if dose reduction can really provide you the same outcomes, then dose reduction is really what's recommended.

Some other considerations with the ESAs. The common dosing regimens are darbepoetin alpha every two to three weeks and epoetin alpha three times per week to once a week. There is a REMS program

that applies to ESAs when they're used for anemia due to cancer chemotherapy. This is called the APPRISE Oncology Program and really it just assists providers and cancer patients with risk information and safe use of ESAs. There's mandatory training enrollment of all healthcare providers that prescribe ESAs and it only applies to the treatment of anemia due to cancer chemotherapy. It doesn't apply to CKD patients.

This brings us to Omontys. Omontys is the most recent ESA to be approved. Sorry, I'm on slide 15. Omontys is indicated for the treatment of anemia due to CKD in adult patients on dialysis. As I stated above, it's dosed once monthly, and it's not indicated, obviously, in nondialysis patients, in patients that are being treated for their anemia due to cancer chemotherapy, and it's obviously not a substitute for RBC transfusions.

Next slide. There we go. So, we're on slide 16. The approval of Omontys was based… or the FDA approval of Omontys was based on the Emerald Clinical Trial program. This is Emerald 1 and 2. This was a 52-week noninferiority study. It focused on the treatment of CKD-associated anemia in dialysis patients who were already on epoetin and obviously these were dialysis patients, and they had to be stable on epoetin alpha or beta prior to enrollment. Hemoglobin levels had to be between 10 and 12, and iron status had to be confirmed, or adequate iron status. It was studied both in IV administration and subQ, as well.

Treatment arms consisted of Omontys once monthly versus treatment of epoetin one to three times per week, and this was based on the prior epoetin dose, and hemoglobin concentrations within the study were specified between 10 and 12. So, that was the target range, 10 and 12. The primary efficacy end points were a mean change in hemoglobin from baseline to evaluation of greater than or equal to negative one, and the safety end point was a composite safety end point of time to first event of death from any cause, MI, adverse events of CHF, unstable angina, and arrhythmia.

Next slide, which is 18. This is the conversion table that was used in the clinical trial and is also in the prescribing information for

Omontys, as well. So, they have some very prespecified conversion table to initiate therapy with Omontys.

Moving onto slide 19, this is the results. It was found that the change from baseline was actually similar between epoetin and Omontys, and Omontys was found to be clinically noninferior to epoetin alpha, and the between group difference was similar as well. The proportion of patients who actually were within the target range was similar between the two treatment groups with a trend towards superiority with epoetin, but it was a nonsignificant difference, and a similar number of patients received blood transfusions.

Slide 20, just to show that when following these patients all the way out to 100 weeks, you can see that the graph… the lines are pretty much superimposed with the epoetin-treated patients and the Omontys-treated patients, and that's in both Emerald 1 and in Emerald 2.

So, slide 21. Moving onto slide 22, there were a similar rate of adverse events between both groups, and when looking at the composite safety endpoint, you can see that the percent of patients with the composite safety endpoint event was similar between the two groups, and it's also broken down by the actual component, as well, which was found to be similar, as well. Now, the reason why we cannot use Omontys in nondialysis patients, and it's only reserved to the dialysis population are due to the results of the Pearl 1 and 2 clinical studies, this was a comparison of Omontys to darbepoetin and this is in nondialysis patients.

Barak Gaster: Next slide.

Vafa Mahboubi: Hello?

Barak Gaster: Advancing the slide for you.

Vafa Mahboubi: Oh, sorry. 23. All right, my apologies. So, the efficacy endpoint was met in both studies. The frequency of the composite safety endpoint, though, was higher in the Omontys group versus the darbepoetin group, and this was a significant difference, and it was really driven by higher rates of death, UA, and arrhythmia.

Moving on, slide 24. Some other considerations. General dosage adjustments apply for Omontys, as with any other ESA in the sense of reducing the dose with nonresponders and increasing the dose by 25% with… sorry, increasing the dose with nonresponders and reducing the dose by 25% if you have a significant rise in hemoglobin. It's contraindicated in patients with uncontrolled hypertension and neurologic, I guess, events did occur, or seizures did occur during clinical trial. So, there is a recommendation to monitor for neurologic symptoms following initiation of therapy, as well.

And that brings us to the end. Sorry about the queuing for the slide. I guess I'm just more used to the WebEx format. My apologies. Are there any questions?

Barak Gaster: It doesn't look like it. Thank you so much for your help, and I think that we can release you now? Yes. Thanks again for all of your help today.

Vafa Mahboubi: Okay, thank you. Bye, bye.

Barak Gaster: Before we get into our discussion, we do have three stakeholders. The first one will be Alex Yang from Affymax and please be ready to speak next, Claire Merinar from Amgen. And I remind you that you have three minutes to speak. Thank you.

Alex Yang: Thank you. Thanks again for the opportunity to present Omontys during this ESA review. As mentioned, just now, Omontys is a new ESA recently approved in March by the FDA for the treatment of CKD anemia in adult patients on dialysis. I will be addressing three points. One is Omontys is approved in dialysis to the clinical safety and efficacy of Omontys similar to other currently available ESAs, and the price of Omontys is parity versus other ESAs. Therefore, we request that the committee place Omontys on formulary with equal parity to Epogen in dialysis.

Number one, the approved indication again. For over two decades in the United States, there has only been one ESA, Epogen, that has been widely available for the U.S. dialysis population. Now, as of earlier this year, dialysis patients and their providers have a choice in ESA

therapy. The approved indication, again, treatment of CKD anemia in adult patients on dialysis. This is the only indication that was sought from the FDA, and therefore the only indication that was approved. It is not approved, as mentioned before, in oncology, not approved for pediatric patients, not approved for CKD patients who are not on dialysis.

Number two, safety and efficacy. As mentioned on the slides already, the clinical safety and efficacy of Omontys in dialysis was demonstrated in two large randomized controlled head-to-head phase-3 trials. Because of the classified safety concerns in the ESA space reported in late 2006, the FDA actually required that the Omontys phase-3 trials be powered for cardiovascular safety. This is the first time ever for any ESA that has ever been done, and these trials represent then the new high bar for safety in the ESA class.

The primary safety evaluation, as mentioned before, are composite cardiovascular safety endpoint, including all cause death, MI, stroke, CHF, unstable angina, and arrhythmia, and this endpoint, as was mentioned, was easily met with a hazard ratio below 1. The primary efficacy endpoint was also easily met demonstrating similar efficacy to Epogen in dialysis.

The third and last point, price parity. The price of Omontys was specifically set at parity with Epogen and dialysis. The most recently available actual individual patient doses for the U.S. dialysis population was used in the calculation. Since then, the price parity has been confirmed numerous times across multiple U.S. dialysis populations.

So, in conclusion:

1. Omontys is approved for adult dialysis patients.
2. The clinical safety and efficacy of Omontys is similar to currently available ESAs.
3. The price of Omontys is at parity.

Therefore, again, we are asking the committee to place Omontys on formulary with equal parity to Epogen. Omontys is the first newest ESA in this patient population for over two decades. Not reimbursing

or covering Omontys would certainly limit providers' choice. Thank you.

Barak Gaster: Thank you, very much. The next speaker is Claire Merinar from Amgen, and please be ready to speak after that, Bob Snediker from Janssen.

Claire Merinar: Thanks, again, for the opportunity to speak with you today. Claire Merinar, medical liaison from Amgen. I am going to take just a couple of minutes to highlight information for Aranesp and Epogen, and I would ask you to please refer to the package inserts for each product for further information.

So, Epogen is an ESA marketed by Amgen for the treatment of anemia associated with CKD in patients on dialysis, and it provides a three times a week dosing that aligns nicely with the three times per week hemodialysis treatment schedule used by the majority of chronic dialysis patients. Three times a week dosing actually allows for timely intervention in terms of managing response to changes in hemoglobin. Patients on dialysis do experience hemoglobin variability due to a number of factors, comorbidities and their current events and practice patterns, which can often be addressed in a timely manner with a three times a week dosing of Epogen.

Aranesp, on the other hand, is a serum half-life approximately three times longer than Epogen and in a nephrology setting, it has FDA approval for the treatment of anemia associated with CKD, including patients on dialysis and not on dialysis. In patients with chronic kidney disease on dialysis, it's dosed once weekly or once every two weeks. A key benefit of Aranesp in patients not on dialysis is that it's administered monthly, thus decreasing the number of injections.

I'll comment briefly on safety, although that was covered earlier. During 2011 in collaboration with the FDA, Amgen did modify the label for Aranesp and Epogen to communicate a realized benefit-risk profile. This information is applicable to all ESAs and the modified PI does include changes to the boxed warning and provides important new information for the treatment of patients with CKD who are on dialysis, as well as those who are not on dialysis and informs of safety risks that have been identified in clinical trials.

In terms of calculating costs in the nephrology setting, there are definitely a number of factors to consider. First of all, there is a nonlinear dose conversion relationship amongst Aranesp versus some of the other ESAs. Different populations with different dose distributions may yield different cost results, and I think it's also well known that there are significant heterogeneity of response, which should also be taken into account.

Lastly, if you think of the recent revisions to the ESA label, including removal of the 10 to 12 hemoglobin target range and reduction or interruption of ESA dosing when hemoglobin levels are above 11 in CKD patients on dialysis or above 10 in CKD patients not on dialysis, and a longer dosing interval for the starting dose of Aranesp in CKD patients not on dialysis. Utilization of ESAs in nephrology is likely to decline given these recent changes to the ESA labels, and historical claims data may not reflect current or future practice patterns, which could influence cost analyses again.

In addition to approval for the treatment of anemia associated with CKD, Aranesp also has approval for treatment of anemia in patients with nonmyeloid malignancies where anemia is due to the effect of concomitant myelosuppressive chemotherapy, and upon initiation, there is a minimum of two additional months of planned chemotherapy.

Barak Gaster: Could you please complete your remarks?

Claire Merinar: Sure. In terms of the oncology setting, I think there are some inherent challenges in terms of dealing with drugs with different dosing, different duration of benefit, different length of therapy, and all of that needs to be taken into account.

So, in summary, I do think Aranesp and Epogen both provide important clinical benefits. Epogen is well matched to the three times a week dosing in dialysis. Aranesp is longer-acting, has multiple indications and dosing intervals, and has been approved for over 10 and 20 years respectively. So, with that, I will finish up. Sorry if I went a little long. Thank you.

Barak Gaster: That's okay. Thank you. Next up is Bob Snediker from Janssen.

Bob Snediker: Thank you, very much. I'll get you all back on schedule. I really don't have much to add to what's already been said. The points that I do want to make evolve around the dosing of Procrit. There are a number of different dosing regimens, although not in the label, have been described in the literature, which may provide advantageous.

Dosing regimens for patients at extended intervals, weekly, every other week, every three weeks, etc. The other point I wanted to make with regards to cost analyses with the ESAs, I think it's important that if you're going to do any kind of cost comparison, it's probably beneficial to look at the cost per course of therapy, i.e. specifically within cancer chemotherapy. Patients are getting dosed per month or whatever the matching intervals are among products. That's perhaps the best way to look at cost comparisons rather than just label to label comparisons, and these have been also described in the literature. That's all I have.

Barak Gaster: Thank you. So, that completes our stakeholder comments. So, now let's move to a review of the cost and drug utilization report that we have before us. Donna, do you want to give us some details on this?

Donna Sullivan: This is Donna Sullivan. The data that is in front of you, again, is from calendar year 2011. What we did in order to try to address the issues about differences in dosing instead of doing a cost per day, which we have done in the past, we have looked at the average cost per user per month knowing that the course of therapy over the course of a year is going to be pretty much continuing for the clients. So, we have the Aranesp. The pharmacy claims, again, is the claims that have gone through our POS system. The other diagnoses, anemia due to chemotherapy, and we have renal failure with dialysis, renal failure without dialysis. Those are the medical claims. So, there are differences in the way that the drugs are priced whether they're medical or pharmacy… dispensed at the pharmacy and that is partially reflective in the pricing that you're seeing in front of you. So, I don't know what else you would like.

Barak Gaster: This is Barak Gaster. Could you speak a little bit more of why there is such a cost disparity in these different groupings?

Donna Sullivan: Really, the only thing that I could tell you is that it's based… so, if you look at the disparity between the medical claims and the pharmacy claims, one is the reimbursement for a medical claim based on our fee schedule, which is not exactly the same as how prescription drugs are priced when they're going through the pharmacy benefit. So, when you're looking at average wholesale price minus a discount, that comes up with a different amount than the fee schedule that the same drug would be applied to if it's filled through the medical benefit. These are also after rebate. So, it's… I don't know if Chuck has any better understanding of the difference between the claims data, but that's really the only understanding that I have.

Chuck Agte: So, one potential difference is within the pharmacy claims, like for example, if you look at Procrit for the pharmacy claims versus the medical ones. The pharmacy claims are going to be a mix of a variety of different diagnoses, so they're not necessarily split out or able to be brought down in terms of the average depending on the dosing based on that particular diagnosis. In terms of the actual difference in specific pricing between them, in general, the drug products that are paid through medical claims are paid at ASP +6%, is it 6 or 7? Somewhere around there, but ASP is average sales price, and those are the same prices that are set by Medicare.

So, that price is set every, I think, quarterly is when we receive the file. So, if there are price fluctuations or increase in prices, those reflect more quickly through pharmacy claims. So, if there's an increase in the average wholesale price, because we pay at AWP -16% through the pharmacy system, and there is not necessarily any direct correlation between average sales price and average wholesale price. So, if there are changes in average wholesale price, those are going to appear more quickly in pharmacy reimbursement than in the physician claim reimbursement. The price is set once sometimes every six months. I do believe we get a file quarterly. So, the price changes happen more quickly with pharmacy.

Barak Gaster: This is Barak Gaster. So, it sounds like the availability of Omontys came after the data period for this report. Can anybody speak to the claim for cost parity?

Donna Sullivan: This is Donna Sullivan. I did not look at the cost of Omontys. Since we were going off just what we had in the claims data, we had no utilization of it within the period. So, I can't confirm or really speak to whether or not it is priced the same, and we would have to look at the rebates that we're getting on it, as well, to… and I'm not even sure that if we do have utilization on it, since it's approval and entrance into the market, whether or not we've actually gotten those rebates back from manufacturers yet so we could even make a cost comparison to the other products.

Barak Gaster: This is Barak Gaster again. If we were to have it on formulary, would it… can you tell us anything about what the potential cost would be, at all? We don't know.

Donna Sullivan: I'm sorry, I don't.

Barak Gaster: Yeah. This is Barak Gaster again. Could you speak one more time? We've covered this before, but, if multiple drugs are on formulary, does Washington State Medicaid have the ability to negotiate a lower price from among the agents that are available?

Chuck Agte: At this point in time, we don't. We are working towards that. Because our supplemental rebate contract is a template that has to be approved by CMS, our current supplemental rebate contract was originally designed for use with the PDL, and unfortunately contains language that makes it specific to the PDL. So, as soon as we're done treading water trying to get a formulary up and running, our next step is to work with CMS to modify our current supplemental rebate agreement so that we can begin seeking supplemental rebates in the future for drugs included in the formulary. So, at this point in time, no. We can't negotiate additional discounts beyond the strict federal rebate, but we are working towards that and hope to be getting there. It takes quite some time for CMS approval sometimes, so we're hoping to get there sometime toward the end of 2013 and at that point would begin looking at negotiating rebates within the context of comparative pricing, but right now we can't.

Barak Gaster: This is Barak Gaster. I think, I mean if we had that in place, then the appeal of having two drugs that seem equally effective that are at least close to cost parity, both on the formulary would be beneficial in terms

of negotiating a contract like that, but we don't have that currently, and we're kind of a sort of murky area, since the only information that we have on the cost of Omontys is what the manufacturer stakeholder has given us today. We really don't know anything other than that.

Chuck Agte: At this point in time, we do have prior authorization on Omontys, because it is a new product. So, one possibility, just to throw out there, is you could consider leaving Omontys on the formulary with our prior authorization criteria, which would allow us to develop cost experience by the time we bring it back to you, and in the meantime, we could closely track it through the PA process.

Deb Wiser: This is Deb Wiser. In looking at the data then, it seems that the Epoetin products are mostly similar in their cost profile and those and the darbepoetin products are equivalent in efficacy and safety, but the darbepoetin products are more expensive. So, I would suggest that we put all of the Epoetin products on formulary, exclude darbepoetin from formulary, and keep the new product, Omontys, on formulary with a PA required.

Susan Rowe: This is Susan Rowe. I have a question, because a lot of these products are given in the physician's office or at a health center. So, I am not sure in terms of how our actions here will reach across that. Will a patient who needs to get a product because of chemotherapy, and they're at their health center, their outpatient chemotherapy clinic, how will this impact that?

Chuck Agte: So, we are, as we are bringing drug classes to you for the formulary… these… some of the ones we brought you today are some of the first that have impact on professionally-administered settings, and the agency's intent is that the decisions you make are applied across all billing settings, and so the impact there would be that like we've done with the drug classes we're hoping to implement soon, we will take a look at, based on any decisions you make for anything that's going nonformulary, we will be going through our data, indentifying both prescribers and clients, each get letters of their own kind regarding the products that they have been taking or have used in the past, which will be nonformulary. So, hopefully with our advanced communication strategies for specific clients and prescribers, as well as our general notifications, then prescribers will be familiar enough to

know what will or will not be nonformulary and it would be like anything else. It would be a prior authorization process. So, they should be aware of, in advance, and if they have a client who needs a product which is nonformulary that they're intending to use, along with their chemotherapy regimen, they should be requesting the nonformulary justification and providing whatever information on why the product that is formulary would not be the right one for their client. So, it's an advanced authorization process like any other. This wouldn't be… there should be enough advance warning built into the process that we don't have somebody showing up for chemotherapy and receiving products that are not formulary. We have a variety of fail-safes built without knowing in advance. We have a variety of fail-safes built into the process where during transition periods we will be approving things one time for clients who have already been on a therapy in the past. We're doing that with all the products within the formulary so that in case there is anything that fell through the cracks in regard to communication, they'd still get another fill of whatever they've been on while we go through another more specific communication at that point to let them know the product is nonformulary.

Barak Gaster: This is Barak Gaster. I would remind us that we're not creating this formulary in a vacuum and that certainly many of the, if not all of the practice settings that we will be impacting, are practice settings in which they have many patients who are dealing with many other formularies, for which almost certainly epoetin is a preferred product over darbepoetin such that I don't think that we're… I think that the likelihood that we will cause a huge disruption is low.

Deb Wiser: This is Deb Wiser. Just as a point, looking at the data, I do see that for renal failure with and without dialysis there are only a few patients that are using Procrit as opposed to Aranesp and without direct experience in that area, I'm not exactly sure if that's something that some providers would feel strongly about.

Christine Klingel: This is Christine Klingel. Yeah, this is really a tough category. I mean, we are counting up a little over a hundred patients that this is affecting, so this is a very small category. Granted, these are very expensive medications, but if they are, I guess one thing for us to consider, too, with the average cost per month, this is only for the drug

and not necessarily any associated office costs. So, for dosing Aranesp less frequently they're probably avoiding office visits, which would have other costs associated. So, while Procrit is a little bit less expensive, Aranesp may be allowing them to extend their visits with providers, which also could add costs. I don't know. My feeling is that I really can't exclude any of these agents based on what we've seen and based on the cost and total number of clients that are affected.

Christopher Smith: This is Christopher Smith, and I would agree with you, Christine. I think that there are advantages to the longer dosing interval in these chronically ill patients and a convenience, unless I'm mistaken, from what I understand today, of the longer-acting Aranesp is significant in this population and something that we have to consider. I think trying to switch all those patients over to Procrit doesn't seem reasonable based on the dosing interval. Is that what the rest of you also understood?

Deb Wiser: This is Deb Wiser. Yeah, I agree. It's a relatively small number of people, and it would be a large number of people to switch.

Chuck Agte: This is Chuck Agte. To continue to… so you guys are aware of your options. Within any drug class, you also have the option of letting us know when you feel the clients should not be switched from an existing therapy. So, if you did have thoughts in regard to… for future patients if there were decisions you thought might be appropriate for new therapies, as opposed to if one of your considerations is not switching clients, you have the option to make decisions and tell us to not switch current clients according to that, though. So, we can grandfather per your direction and continue existing therapies that worked for clients before but have a different standard for new starts, if that's something that's appropriate for the board to consider.

Susan Rowe: This is Susan Rowe. So, if we were to pursue that kind of avenue and have you report back to us on what the use is with existing clients, new starts, would we get the full information that Christine's alluding to that it's not just the drug cost but the number of appointments also? I'm just trying to think if we were to do something like that, would we get the information back to make a more educated decision?

Chuck Agte: We've been working on a cost model that included the costs of related office visits, etc. I don't know if that got included in this final version or if we're still working that out.

Donna Sullivan: We're still working that out.

Chuck Agte: Okay. So, we are in process for exactly that kind of cost analysis. There's all kinds of layers of difficulty to identifying when an office visit charge would be appropriate to include or not. That is part of the difficulty of the model, because if they're there for chemotherapy anyway, you don't want to attribute the cost of that visit to this particular drug. If they're getting administration of other products. If they're not, and this were to be the only thing administered at that particular visit, then we would include it, and so that's part of the fine level of detail that we're trying to get into that we haven't put together into a full cost model yet.

Susan Rowe: Okay. Thank you.

Barak Gaster: This is Barak Gaster. I think it is the disparity in number of clients by diagnosis that was pointed out is, you know, it's a four- to ten-fold difference between the two renal failure diagnoses that I think does suggest to us that there may be clinical considerations that we are not aware of and that we may not want to make motion decisions about until we understand better.

Deb Wiser: This is Deb Wiser. We may, at one point, want to differentiate between the dialysis and nondialysis patients, too, because the dialysis patients are in three times a week generally and at least two times a week, whereas the nondialysis patients may be as more of a routine may be put on the Aranesp… sorry, reverse. So, the people who are on dialysis may be getting Aranesp just because of habit, as opposed to the people who are not on dialysis. It would be truly more convenient, because they wouldn't otherwise have to come in.

Barak Gaster: This is Barak Gaster. I think that we are coming to some consensus that we need more clinical background information about this drug class before making the decision about it. So, I think that is where we're going to have to leave this for now if there is no more discussion.

Chuck Agte: So, we can continue to develop pricing and claims model and have a better view of Omontys, as well, hopefully in the near future, what kind of, and I'm anticipating… and maybe I shouldn't be asking this one, because it's probably a Donna question, but what kind of additional clinical information do you believe the board needs to move forward?

Barak Gaster: This is Barak Gaster. I mean, this bumps up exactly against the discussion that we had as we embarked on this whole formulary process, which is where to get good, free-of-bias, sort of clinical expertise, and I think this is a class of medications that no one on this committee routinely prescribes. It's a very niche… this is a very niche area of medicine that having an oncologist and a nephrologist who we felt confident was free of financial ties would be useful to us. I don't think that the monograph fully sort of flushed out what the clinical differences would be that might be taken into consideration between these two drugs. So, I think if we were… I mean, ideally we would have a nephrologist and/or an oncologist speak to us.

Chuck Agte: I think the agency can work towards identifying options for that, at least in terms of oncology. We do have Medicaid staff in house. Not to be confused with our chief medical officer, our senior what is the term for them, our physician consultants. Our senior medical consultant that we have currently is a pediatric oncologist. So, we do have some oncology resources and I believe the agency could work toward identifying other resources, as well. So, what it sounds like to me is you're requesting unbiased expert testimony of some kind?

Barak Gaster: Yeah.

Susan Rowe: This is Susan Rowe. I also, I guess I… if we had better definition to the pharmacy claims of what those diagnoses were, I think it might be helpful to us. So, earlier in the year we talked about trying to get a firmer diagnosis on the use of our stimulant drugs. Is that an option?

Chuck Agte: Yes, along with, like I said, the cost model that we're working on to try and figure out the ancillary charges of physician claims, we are also working towards merging… basically, pulling some more diagnostic information on those things which are purely pharmacy claims at this

moment. Again, there are difficulties in mining the medical claim data to make sure they are associated correctly, but we are working towards that.

In regard to the ADHD medications, that is more of a manual process basically and what we'll be bringing back to you, simply because anything that does come in for prior authorization, because it has a diagnosis other than ADHD, Nicole is personally looking at all of those. So, Nicole will be able to report that out from actual direct experience whereas this would be more of a data approach, because they aren't all on full prior authorization at the moment, but it's something that we can definitely look at pulling together.

Susan Rowe: Thank you.

Barak Gaster: Any other questions or thoughts? All right. And so, now we move to discussing drug class selection for the December meeting, Donna.

Donna Sullivan: Okay. I'm not sure what the process is. Do you have to affirmly decide that you're tabling this until the next meeting, or do you want this to try to come back for the December meeting?

Barak Gaster: Yeah, so this is Barak Gaster. I think that we feel like we have explored this drug class as much as we can currently with the information that we have in front of us and are requesting more information, and whether that information could come to us at the December meeting or at the February meeting, we would be happy to review it again with more information.

Susan Rowe: I can move. This is Susan Rowe. I can move to table this until more information is available in December or February.

Donna Sullivan: Thank you.

Deb Wiser: Deb Wiser, I second.

Barak Gaster: All in favor say, aye.

Group: Aye.

Barak Gaster: All opposed, same sign. So, that strong motion passes.

Donna Sullivan: So, this is Donna Sullivan. So, moving forward to what we have for December and what I can get available for you for December, we have the possibility of five drug classes that can be ready to go between December and February. Actually, there are six. I left one off, the anticonvulsants. So, I have the monographs for the growth hormones and the ophthalmic prostaglandins pretty much ready to go so that we can get those posted, and the second one is the benign prostatic hypertrophy. The monograph is a little dated. It's from 2009, I believe, and so we would probably be trying to update that with some compendia information, as well, which will be a little bit more difficult for us to get prepared, because of the staffing resources. The benign prostatic hypertrophy, I just mentioned that one, I'm sorry. The pulmonary arterial hypertension, I believe, is also a 2010, as well as the pancreatic enzymes. So, my suggestion, really, is to go with growth hormones and the ophthalmic prostaglandins for December, and we can hopefully get the data that you are requesting for the erythropoietin-stimulating agents together before then as well.

Then, tackling… I would like to tackle the anticonvulsants in February. That's when MedImpact's clinical consultant that does the anticonvulsant class reviews will be back from maternity leave at that time, so we would like to do that in February, in addition to potentially the pulmonary hypertension medications and the BPH drugs.

Barak Gaster: Okay. This is Barak Gaster. I think probably the expertise on the committee in terms of prescribing is going to be very high for the BPH drugs and very low for the other four.

Donna Sullivan: Okay.

Barak Gaster: So, I think that today's discussion about the erythropoietin-stimulating agents brings up a concern that we may end up in similar sort of murky water about making decisions that we have less expertise to sort of really hang our hat on, but we are certainly happy to review monographs and see where we can get to.

Donna Sullivan: Okay.

Barak Gaster: We can review the DUR data and look at the monographs and see if we can come to conclusions, but I think the BPH drugs is a natural one that probably fits with many of the clinicians on the panel in terms of helping to guide decision making.

Donna Sullivan: So, you'd like to see that in December if you can? Is that what you're asking?

Barak Gaster: That would be my preference.

Donna Sullivan: Okay.

Deb Wiser: I would feel more productive.

Donna Sullivan: Okay. We will do that then.

Barak Gaster: Great. Excellent.

Susan Rowe: So, this is Susan Rowe. We've decided on the drug categories, and I'm wondering about some of the other DUR things that we usually do, and we have… we've been working really hard on the formulary. So, in terms of bringing back some of the other safety concerns that we've been talking about earlier in the year…

Donna Sullivan: So, what we've been doing is we have been working on looking at the top 20 narcotic prescribers again. We have the data pulled, and I just haven't had a chance to compare where they are, since the last time we reviewed them for next year. So, that is one thing that we were also going to probably bring back in December, if we're able to get the information compiled and ready to go, and I believe Chuck and Nicole have also been preparing… or have a list of things on their agenda that they need to bring to the board, as well, for consideration. So, Chuck, do you have an idea of what you might be bringing?

Chuck Agte: Yes. One of the things that we hope to bring in the near future is, because basically we're trying to get to the followup on the top 20 narcotic prescribers next. We have a new indication for Truvada that is a new indication, which we believe we need the board's input on policy direction, as far as where we want to go in terms of preventative use and off the top of my head, I think we had something else, and

we'll get back to you. I have a couple of things on a list at my desk, which off the top of my head I was not prepped for advanced warning on what we're trying to bring to you next, but those would be the next two main things is the followup on the opioid prescribers and then seeking your guidance in regard to preventative use for HIV medications.

Barak Gaster: Thank you. All right, so with that, I think we can convene today's DUR meeting, and thank you all very much.